EXHIBIT 2

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (GBW) **DEMAND FOR JURY TRIAL**
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC. Plaintiff/Counter-Defendants.	[redacted] REDACTED - PUBLIC VERSION

DEFENDANT SAREPTA THERAPEUTICS, INC.'S ~~FIRST~~SECOND AMENDED ANSWER, DEFENSES, AND COUNTERCLAIMS TO PLAINTIFF NIPPON SHINYAKU CO., LTD.'S SECOND AMENDED COMPLAINT

Defendant Sarepta Therapeutics, Inc. ("Sarepta"), by and through its undersigned counsel, hereby submits its Answer and Defenses to Plaintiff Nippon Shinyaku Co., Ltd.'s ("Nippon Shinyaku") Second Amended Complaint for Breach of Contract, Declaratory Judgment of Patent Invalidity, and Patent Infringement ("SAC") (D.I. 86), filed January 14, 2022. In addition, Sarepta and The University of Western Australia ("UWA") assert the amended counterclaims below against Nippon Shinyaku and its wholly owned U.S. subsidiary, NS Pharma, Inc. ("NS Pharma").

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ANSWER

Nature of the Action[1]

1. Sarepta admits that the SAC purports to assert a claim for breach of contract. Sarepta admits that it entered into a Mutual Confidentiality Agreement ("MCA") with Nippon Shinyaku. Sarepta admits that it filed seven petitions for *inter partes* review (collectively, the "IPR Petitions") with the Patent Trial and Appeal Board ("PTAB") of the United States Patent and Trademark Office ("USPTO"), challenging the patentability of all claims of Nippon Shinyaku's U.S. Patent Nos. 9,708,361 ("the '361 patent"); 10,385,092 ("the '092 patent); 10,407,461 ("the '461 patent"); 10,487,106 ("the '106 patent"); 10,647,741 ("the '741 patent"); 10,662,217 ("the '217 patent"); and 10,683,322 ("the '322 patent) (collectively, "the NS Patents").[2] Sarepta denies any remaining allegations in Paragraph 1.

2. Sarepta admits that the SAC purports to assert claims for declaratory judgment of invalidity of the University of Western Australia's ("UWA") U.S. Patent Nos. 9,994,851 ("the '851 patent"); 10,227,590 ("the '590 patent"); and 10,266,827 ("the '827 patent") (collectively, "the UWA Patents"). Sarepta admits that it has exclusive rights to the UWA Patents for the treatment of muscular dystrophies and the right to enforce the UWA Patents. Sarepta denies any remaining allegations in Paragraph 2.

3. Sarepta admits that the SAC further purports to assert claims for infringement of the NS Patents. Sarepta admits that it developed golodirsen (SRP-4053) and has marketed it as

[1] For convenience and clarity, Sarepta's Answer uses the same headings as the SAC. Sarepta does not admit any allegations contained in the SAC's headings.

[2] *See Sarepta Therapeutics, Inc. v. Nippon Shinyaku Co., Ltd.*, IPR2021-01134 (U.S. Patent No. 9,708,361); IPR2021-01135 (U.S. Patent No. 10,385,092); IPR2021-01136 (U.S. Patent No. 10,407,461); IPR2021-01137 (U.S. Patent No. 10,487,106); IPR2021-01138 (U.S. Patent No. 10,647,741); IPR2021-01139 (U.S. Patent No. 10,662,217); IPR2021-01140 (U.S. Patent No. 10,683,322).

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Vyondys 53® in the United States. Sarepta admits that Vyondys 53® is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer subclass that induces skipping of exon 53 of the human dystrophin gene to treat Duchenne Muscular Dystrophy ("DMD"). Sarepta denies any remaining allegations in Paragraph 3.

Parties

4. Upon information and belief, Sarepta admits the allegations in Paragraph 4.

5. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 5 and therefore denies them.

6. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 6 and therefore denies them.

7. Sarepta admits the allegations in Paragraph 7.

Jurisdiction and Venue

8. Paragraph 8 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that the SAC purports to assert a breach of contract claim under Delaware law. Sarepta denies any remaining allegations in Paragraph 8.

9. Paragraph 9 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that the SAC purports to assert a claim for declaratory judgment of invalidity of the UWA Patents under the Patent Laws of the United States, 35 U.S.C. §§ 1 *et seq.*, and under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 *et seq.* Sarepta denies any remaining allegations in Paragraph 9.

10. Paragraph 10 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta denies that the Court has subject matter jurisdiction over Claim I (Breach of Contract) and Claim II of the SAC (Declaratory Judgment of Invalidity of the

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UWA Patents). For purposes of this action only, Sarepta does not contest that the Court has subject matter jurisdiction over Claims III-IX of the SAC. Sarepta denies any remaining allegations in Paragraph 10.

11. Sarepta admits that it competes with Nippon Shinyaku in developing and commercializing exon 53 skipping therapies for the treatment of DMD in patients amenable to exon 53 skipping in the United States. Upon information and belief, Sarepta admits that Sarepta and Nippon Shinyaku are the only companies with approval from the U.S. Food and Drug Administration ("FDA") to market oligonucleotide therapies for the treatment of DMD in patients amenable to exon 53 skipping in the United States. Sarepta admits that its Vyondys 53® (golodirsen) product was approved by the FDA. Upon information and belief, Sarepta admits that Nippon Shinyaku's Viltepso (viltolarsen) product was subsequently approved by the FDA. Sarepta denies any remaining allegations in Paragraph 11.

12. Paragraph 12 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that the UWA was granted U.S. Patent Nos. 8,455,636 ("the '636 patent") and 9,024,007 ("the '007 patent"), entitled "Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof." Sarepta admits that the '636 and '007 patents were issued by the USPTO on June 4, 2013 and May 5, 2015, respectively. Sarepta admits that the claims of the '636 and '007 patents cover Sarepta's Vyondys 53® (golodirsen) product. Sarepta denies any remaining allegations in Paragraph 12.

13. Paragraph 13 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that the UWA Patents are listed in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") for Vyondys 53®. Sarepta admits that the Orange Book lists a patent expiry date of June 28, 2025 for

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the UWA Patents. Sarepta admits that it has submitted applications for patent term extension for the UWA Patents. Sarepta denies any remaining allegations in Paragraph 13.

14. Sarepta denies the allegations in Paragraph 14.

15. Sarepta admits that Matthew Gall of Sarepta attended a meeting with Masaya Toda of Nippon Shinyaku on or about January 13, 2020 to discuss a potential business relationship between Sarepta and Nippon Shinyaku. Sarepta is without sufficient knowledge or information to form a belief as to what Nippon Shinyaku understood the parties to have discussed, and therefore denies the same. Sarepta denies any remaining allegations in Paragraph 15.

16. Sarepta admits that Chris Verni, Sarepta's Chief IP counsel, spoke with Nippon Shinyaku's outside counsel on or about January 28, 2020 while attending a conference for the Association of Corporate Patent Counsel. Sarepta denies any remaining allegations in Paragraph 16.

17. Sarepta admits that, after June 1, 2021, it had not granted Nippon Shinyaku a license or covenant not to sue for the UWA Patents, and Nippon Shinyaku had not granted Sarepta a license or covenant not to sue for the NS Patents. Sarepta denies any remaining allegations in Paragraph 17.

18. Sarepta admits that on or about July 6, 2021, Joe Zenkus of Sarepta sent an email to Masaya Toda of Nippon Shinyaku regarding Sarepta's filing of the IPR petitions challenging the patentability of the NS Patents. Sarepta admits that Paragraph 18 quotes a portion of Nippon Shinyaku's Exhibit D.I. 39-4 (with alteration to original). Sarepta denies any remaining allegations in Paragraph 18.

19. Paragraph 19 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 19 quotes (with emphasis added) a

portion of Nippon Shinyaku's Exhibit D.I. 39-4. Sarepta is without sufficient knowledge or information to form a belief as to Nippon Shinyaku's beliefs, and therefore denies the same. Sarepta denies any remaining allegations in Paragraph 19.

20. Sarepta admits that on or about September 8, 2021, Nippon Shinyaku sent Sarepta a proposed covenant not to sue Nippon Shinyaku for infringement of the UWA Patents, which Nippon Shinyaku requested that Sarepta execute and return to Nippon Shinyaku no later than the close of business on September 10, 2021. Sarepta admits that it did not execute the proposed covenant not to sue. Sarepta denies any remaining allegations in Paragraph 20.

21. Paragraph 21 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Nippon Shinyaku's SAC purports to assert claims for patent infringement of the NS Patents under the Patent Laws of the United States, 35 U.S.C. §§ 1 *et seq.* Sarepta denies any remaining allegations in Paragraph 21.

22. Paragraph 22 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Nippon Shinyaku's SAC alleges that the amount in controversy exceeds $75,000, exclusive of interest and costs. Sarepta denies any remaining allegations in Paragraph 22.

23. Sarepta admits that it markets, offers to sell, and/or sells Vyondys 53® in the United States, including in Delaware. Sarepta denies any remaining allegations in Paragraph 23.

24. Paragraph 24 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 24 alleges that this Court has subject matter jurisdiction over Nippon Shinyaku's patent infringement claims under 28 U.S.C. §§ 1331 and 1338(a). For purposes of this action only, Sarepta does not contest that the Court has subject

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matter jurisdiction over those patent infringement claims. Sarepta denies any remaining allegations in Paragraph 24.

25. Paragraph 25 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that it is a Delaware corporation. Sarepta does not contest that this Court has personal jurisdiction over it for purposes of this action only. Sarepta denies any remaining allegations in Paragraph 25.

26. Paragraph 26 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that it is a Delaware corporation. Sarepta does not contest that venue is proper in the District of Delaware for purposes of this action only. Sarepta denies any remaining allegations in Paragraph 26.

Duchenne Muscular Dystrophy

27. Sarepta admits that DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness, which primarily affects boys but in rare cases can affect girls. Sarepta admits that DMD often occurs in people without a known family history of the condition. Sarepta admits that DMD occurs in about one out of every 3,600 male infants worldwide and is the most common type of muscular dystrophy. Sarepta admits that the first symptoms usually present between three- and five-years old and worsen over time. Sarepta admits that patients with DMD progressively lose the ability to perform everyday activities and often require a wheelchair and assistance by their early teens. Sarepta admits that as DMD progresses, life-threatening heart and respiratory conditions can occur, and patients, although disease severity and life expectancy vary, typically die of the disease in their 20s or 30s. Sarepta denies any remaining allegations in Paragraph 27.

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28. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 28 and therefore denies them.

29. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 29 and therefore denies them.

30. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 30 and therefore denies them.

31. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 31 and therefore denies them.

32. Sarepta admits that in Becker Muscular Dystrophy (BMD), in-frame mutations in the dystrophin gene result in truncated but functional dystrophin. Sarepta admits that BMD patients typically experience milder symptoms than DMD patients, ranging from borderline DMD to no symptoms at all. Sarepta denies any remaining allegations in Paragraph 32.

33. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 33 and therefore denies them.

Exon-Skipping Antisense Oligomers as a Therapeutic Option

34. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 34 and therefore denies them.

35. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 35 and therefore denies them.

Nippon Shinyaku's Development of Exon 53 Skipping Oligomers

36. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 36 and therefore denies them.

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37. Upon information and belief, Sarepta admits that Nippon Shinyaku purports to have filed Japanese Patent Application No. 2010-196032 with the National Center of Neurology and Psychiatry ("NCNP") on September 1, 2010. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the remaining matters asserted in Paragraph 37 and therefore denies them.

38. Upon information and belief, Sarepta admits that Nippon Shinyaku obtained approval in Japan and the United States for Viltepso. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the remaining matters asserted in Paragraph 38 and therefore denies them.

The NS Patents-In-Suit

39. Sarepta admits that the '361 patent is entitled "Antisense Nucleic Acids" and states that it was issued on July 18, 2017. Sarepta admits that the '361 patent lists, on its face, Nippon Shinyaku and NCNP as assignees, and Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata as inventors. Sarepta admits that Nippon Shinyaku's Exhibit D.I. 2-2 purports to be a copy of the '361 patent. Sarepta denies that the '361 patent is valid or enforceable. Sarepta denies any remaining allegations in Paragraph 39.

40. Sarepta admits that the '092 patent is entitled "Antisense Nucleic Acids" and states that it was issued on August 20, 2019. Sarepta admits that the '092 patent lists, on its face, Nippon Shinyaku and NCNP as assignees, and Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata as inventors. Sarepta admits that Nippon Shinyaku's Exhibit D.I. 2-3 purports to be a copy of the '092 patent. Sarepta denies that the '092 patent is valid or enforceable. Sarepta denies any remaining allegations in Paragraph 40.

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41. Sarepta admits that the '461 patent is entitled "Antisense Nucleic Acids" and states that it was issued on September 10, 2019. Sarepta admits that the '461 patent lists, on its face, Nippon Shinyaku and NCNP as assignees, and Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata as inventors. Sarepta admits that Nippon Shinyaku's Exhibit D.I. 2-4 purports to be a copy of the '461 patent. Sarepta denies that the '461 patent is valid or enforceable. Sarepta denies any remaining allegations in Paragraph 41.

42. Sarepta admits that the '106 patent is entitled "Antisense Nucleic Acids" and states that it was issued on November 26, 2019. Sarepta admits that the '106 patent lists, on its face, Nippon Shinyaku and NCNP as assignees, and Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata as inventors. Sarepta admits that Nippon Shinyaku's Exhibit D.I. 2-5 purports to be a copy of the '106 patent. Sarepta denies that the '106 patent is valid or enforceable. Sarepta denies any remaining allegations in Paragraph 42.

43. Sarepta admits that the '741 patent is entitled "Antisense Nucleic Acids" and states that it was issued on May 12, 2020. Sarepta admits that the '741 patent lists, on its face, Nippon Shinyaku and NCNP as assignees, and Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata as inventors. Sarepta admits that Nippon Shinyaku's Exhibit D.I. 2-6 purports to be a copy of the '741 patent. Sarepta denies that the '741 patent is valid or enforceable. Sarepta denies any remaining allegations in Paragraph 43.

44. Sarepta admits that the '217 patent is entitled "Antisense Nucleic Acids" and states that it was issued on May 26, 2020. Sarepta admits that the '217 patent lists, on its face, Nippon Shinyaku and NCNP as assignees, and Naoki Watanabe, Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata as inventors. Sarepta admits that Nippon Shinyaku's Exhibit D.I. 2-7 purports to

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be a copy of the ’217 patent. Sarepta denies that the ’217 patent is valid or enforceable. Sarepta denies any remaining allegations in Paragraph 44.

45. Sarepta admits that the ’322 patent is entitled “Antisense Nucleic Acids” and states that it was issued on June 16, 2020. Sarepta admits that the ’322 patent lists, on its face, Nippon Shinyaku and NCNP as assignees, and Naoki Watanabe, Youhei Satou, Shin’ichi Takeda, and Tetsuya Nagata as inventors. Sarepta admits that Nippon Shinyaku’s Exhibit D.I. 2-8 purports to be a copy of the ’322 patent. Sarepta denies that the ’322 patent is valid or enforceable. Sarepta denies any remaining allegations in Paragraph 45.

46. Paragraph 46 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Nippon Shinyaku’s Exhibit D.I. 39-5 purports to be a license agreement between Nippon Shinyaku and NCNP. Sarepta is without knowledge or information sufficient to form a belief as to the truth of the remaining matters asserted in Paragraph 46 and therefore denies them.

47. Paragraph 47 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 47 and therefore denies them.

48. Paragraph 48 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta is without knowledge or information sufficient to form a belief as to the truth of the matters asserted in Paragraph 48 and therefore denies them.

The UWA Patents

49. Sarepta admits that, on June 12, 2018, the ’851 patent entitled “Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof” issued to UWA as assignee with named inventors Stephen Donald Wilton, Sue Fletcher, and Graham McClorey.

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Sarepta admits that it has exclusive rights to the '851 patent for the treatment of muscular dystrophies and the right to enforce the '851 patent. Sarepta denies any remaining allegations in Paragraph 49.

50. Sarepta admits that, on March 12, 2019, the '590 patent entitled "Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof" issued to UWA as assignee with named inventors Stephen Donald Wilton, Sue Fletcher, and Graham McClorey. Sarepta admits that it has exclusive rights to the '590 patent for the treatment of muscular dystrophies and the right to enforce the '590 patent. Sarepta denies any remaining allegations in Paragraph 50.

51. Sarepta admits that, on April 23, 2019, the '827 patent entitled "Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof" issued to UWA as assignee with named inventors Stephen Donald Wilton, Sue Fletcher, and Graham McClorey. Sarepta admits that it has exclusive rights to the '827 patent for the treatment of muscular dystrophies and the right to enforce the '827 patent. Sarepta denies any remaining allegations in Paragraph 51.

Sarepta's Infringing Product

52. Paragraph 52 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Vyondys 53® is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer subclass that contains 25 linked subunits and is designed to bind to exon 53 of human dystrophin pre-RNA. Sarepta denies any remaining allegations in Paragraph 52.

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53. Sarepta admits that Vyondys 53® is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing. Sarepta denies any remaining allegations in Paragraph 53.

54. Paragraph 54 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Vyondys 53® is administered to patients and is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with a genetic mutation that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 54.

55. Sarepta denies the allegations in Paragraph 55.

56. Sarepta admits that it sponsored clinical trials in the United States for Vyondys 53® (golodirsen). Sarepta denies any remaining allegations in Paragraph 56.

57. Sarepta admits that the FDA issued a press release on December 12, 2019, stating that it granted accelerated approval of Vyondys® 53 (golodirsen) to treat DMD patients who have a confirmed mutation of the dystrophin gene amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 57.

58. Sarepta admits that on December 12, 2019, it issued a press release containing a statement partially quoted in Paragraph 58. Sarepta denies any remaining allegations in Paragraph 58.

59. Paragraph 59 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that, following FDA approval, it has marketed, offered to sell, and/or sold Vyondys 53® in the United States for the treatment of DMD patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta admits that its Form 10-K Annual Report for 2020 refers to Vyondys 53® as a commercial

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product and states that Vyondys 53® was sold in 2020 and 2019. Sarepta denies any remaining allegations in Paragraph 59.

60. Paragraph 60 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that it markets, offers to sell, and/or sells Vyondys 53® in the United States for the treatment of DMD patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 60.

Sarepta's Breach of the MCA

61. Sarepta admits the allegations in Paragraph 61.

62. Paragraph 62 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 62 quotes a portion of Section 6.1 of the MCA. Sarepta denies any remaining allegations in Paragraph 62.

63. Paragraph 63 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 63 quotes a portion of Section 10 of the MCA. Sarepta denies any remaining allegations in Paragraph 63.

64. Paragraph 64 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 64 quotes from the MCA's definition of "Potential Actions" in Section 1. Sarepta denies any remaining allegations in Paragraph 64.

65. Paragraph 65 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 65 quotes from the MCA's definitions of "Covenant Term" and "Term" in Section 1. Sarepta denies any remaining allegations in Paragraph 65.

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66. Sarepta admits that it filed the IPR Petitions with the PTAB on June 21, 2021, challenging the patentability of all claims of the NS Patents. Sarepta denies any remaining allegations in Paragraph 66.

CLAIM I
(Breach of Contract)

67. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

68. Paragraph 68 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta denies that the MCA is valid or enforceable under Nippon Shinyaku's legally erroneous contract interpretation. Sarepta denies any remaining allegations in Paragraph 68.

69. Sarepta admits that Paragraph 69 quotes from a portion of one sentence in Section 10 of the MCA. Sarepta denies any remaining allegations in Paragraph 69.

70. Sarepta admits that Paragraph 70 quotes the MCA's definition of "Potential Actions" in Section 1. Sarepta denies any remaining allegations in Paragraph 70.

71. Sarepta admits that it filed the IPR Petitions with the PTAB on June 21, 2021, challenging the patentability of all claims of the NS Patents. Sarepta denies any remaining allegations in Paragraph 71.

72. Sarepta denies the allegations in Paragraph 72.

73. Sarepta denies the allegations in Paragraph 73.

74. Sarepta denies the allegations in Paragraph 74.

75. Sarepta denies the allegations in Paragraph 75.

CLAIM II
(Declaratory Judgment of Invalidity of the UWA Patents)

76. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

[redacted]

77. Sarepta admits that it competes with Nippon Shinyaku in developing and commercializing exon 53 skipping therapies for the treatment of DMD in patients amenable to exon 53 skipping in the United States. Upon information and belief, Sarepta admits that Sarepta and Nippon Shinyaku are the only companies with approval from the FDA to market oligonucleotide therapies for the treatment of DMD in patients amenable to exon 53 skipping in the United States. Sarepta admits that its Vyondys 53® (golodirsen) product was approved by the FDA. Upon information and belief, Sarepta admits that Nippon Shinyaku's Viltepso (viltolarsen) product was subsequently approved by the FDA. Sarepta denies any remaining allegations in Paragraph 77.

78. Paragraph 78 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that UWA was granted the '636 patent and the '007 patent, each entitled "Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof." Sarepta admits that the '636 and '007 patents were issued by the USPTO on June 4, 2013 and May 5, 2015, respectively. Sarepta admits that the claims of the '636 and '007 patents cover Sarepta's Vyondys 53® (golodirsen) product. Sarepta denies any remaining allegations in Paragraph 78.

79. Paragraph 79 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that the UWA Patents are listed in the FDA Orange Book for Vyondys 53®. Sarepta admits that the Orange Book lists a patent expiry date of June 28, 2025 for the UWA Patents. Sarepta admits that it has submitted applications for patent term extension for the UWA Patents. Sarepta denies any remaining allegations in Paragraph 79.

80. Sarepta denies the allegations in Paragraph 80.

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81. Sarepta admits that Matthew Gall of Sarepta attended a meeting with Masaya Toda of Nippon Shinyaku on or about January 13, 2020 to discuss a potential business relationship between Sarepta and Nippon Shinyaku. Sarepta is without sufficient knowledge or information to form a belief as to what Nippon Shinyaku understood the parties to have discussed, and therefore denies the same. Sarepta denies any remaining allegations in Paragraph 81.

82. Sarepta admits that Chris Verni, Sarepta's Chief IP counsel, spoke with Nippon Shinyaku's outside counsel on or about January 28, 2020 while attending a conference for the Association of Corporate Patent Counsel. Sarepta denies any remaining allegations in Paragraph 82.

83. Sarepta admits that, after June 1, 2021, it had not granted Nippon Shinyaku a license or covenant not to sue for the UWA Patents, and Nippon Shinyaku had not granted Sarepta a license or covenant not to sue for the NS Patents. Sarepta denies any remaining allegations in Paragraph 83.

84. Sarepta admits that on or about July 6, 2021, Joe Zenkus of Sarepta sent an email to Masaya Toda of Nippon Shinyaku regarding Sarepta's filing of the IPR petitions challenging the patentability of the NS Patents. Sarepta admits that Paragraph 84 quotes a portion of Nippon Shinyaku's Exhibit D.I. 39-4. Sarepta denies any remaining allegations in Paragraph 84.

85. Paragraph 85 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 85 quotes (with emphasis added) a portion of Nippon Shinyaku's Exhibit D.I. 39-4. Sarepta is without sufficient knowledge or information to form a belief as Nippon Shinyaku's beliefs, and therefore denies the same. Sarepta denies any remaining allegations in Paragraph 85.

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86. Sarepta admits that on or about September 8, 2021, Nippon Shinyaku sent Sarepta a proposed covenant not to sue Nippon Shinyaku for infringement of the UWA Patents, which Nippon Shinyaku requested that Sarepta execute and return to Nippon Shinyaku no later than the close of business on September 10, 2021. Sarepta admits that it did not execute the proposed covenant not to sue. Sarepta denies any remaining allegations in Paragraph 86.

87. Sarepta denies the allegations in Paragraph 87.

88. Sarepta denies the allegations in Paragraph 88.

89. Sarepta denies the allegations in Paragraph 89.

90. Sarepta denies the allegations in Paragraph 90.

91. Sarepta denies the allegations in Paragraph 91.

CLAIM III
(Infringement of the '361 Patent)

92. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

93. Sarepta admits that Paragraph 93 quotes claim 1 of the '361 patent.

94. Sarepta admits that Paragraph 94 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 11." Sarepta admits that golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. Sarepta denies any remaining allegations in Paragraph 94.

95. Sarepta admits that Paragraph 95 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 12.1." Sarepta admits that golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with a genetic mutation that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 95.

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96. Sarepta admits that Paragraph 96 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 12.1." Sarepta admits that the sequence of bases from the 5' end to 3' end of golodirsen is GTTGCCTCCGGTTCTGAAGGTGTTC. Sarepta denies any remaining allegations in Paragraph 96.

97. Sarepta denies the allegations in Paragraph 97.

98. Sarepta denies the allegations in Paragraph 98.

99. Paragraph 99 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 99 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 1." Sarepta admits that Vyondys 53® is indicated for the treatment of DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 99.

100. Sarepta denies the allegations in Paragraph 100.

101. Paragraph 101 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 101 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 1; Highlights of Prescribing Information (Feb. 11, 2021) § 1." Sarepta admits that Vyondys 53® is indicated for the treatment of DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 101.

102. Sarepta denies the allegations in Paragraph 102.

103. Sarepta denies the allegations in Paragraph 103.

104. Sarepta denies the allegations in Paragraph 104.

[redacted]

CLAIM IV
(Infringement of the '092 Patent)

105. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

106. Sarepta admits that Paragraph 106 quotes claim 1 of the '092 patent.

107. Sarepta admits that Paragraph 107 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 11." Sarepta admits that golodirsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. Sarepta admits that golodirsen contains 25 linked subunits. Sarepta denies any remaining allegations in Paragraph 107.

108. Sarepta admits that Paragraph 108 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) §11." Sarepta admits that the sequence of bases of golodirsen from the 5' end to 3' end is GTTGCCTCCGGTTCTGAAGGTGTTC. Sarepta denies any remaining allegations in Paragraph 108.

109. Paragraph 109 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta denies the allegations in Paragraph 109.

110. Sarepta admits that Paragraph 110 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 12.1." Sarepta admits that golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with a genetic mutation that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 110.

111. Sarepta denies the allegations in Paragraph 111.

112. Sarepta denies the allegations in Paragraph 112.

113. Paragraph 113 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 113 purports to quote in part from

[redacted]

"Highlights of Prescribing Information (Dec. 12, 2019) § 1." Sarepta admits that Vyondys 53® is indicated for the treatment of DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 113.

114. Sarepta denies the allegations in Paragraph 114.

115. Paragraph 115 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 115 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 1; Highlights of Prescribing Information (Feb. 11, 2021) § 1." Sarepta admits that Vyondys 53® is indicated for the treatment of DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 115.

116. Sarepta denies the allegations in Paragraph 116.

117. Sarepta denies the allegations in Paragraph 117.

118. Sarepta denies the allegations in Paragraph 118.

CLAIM V
(Infringement of the '461 Patent)

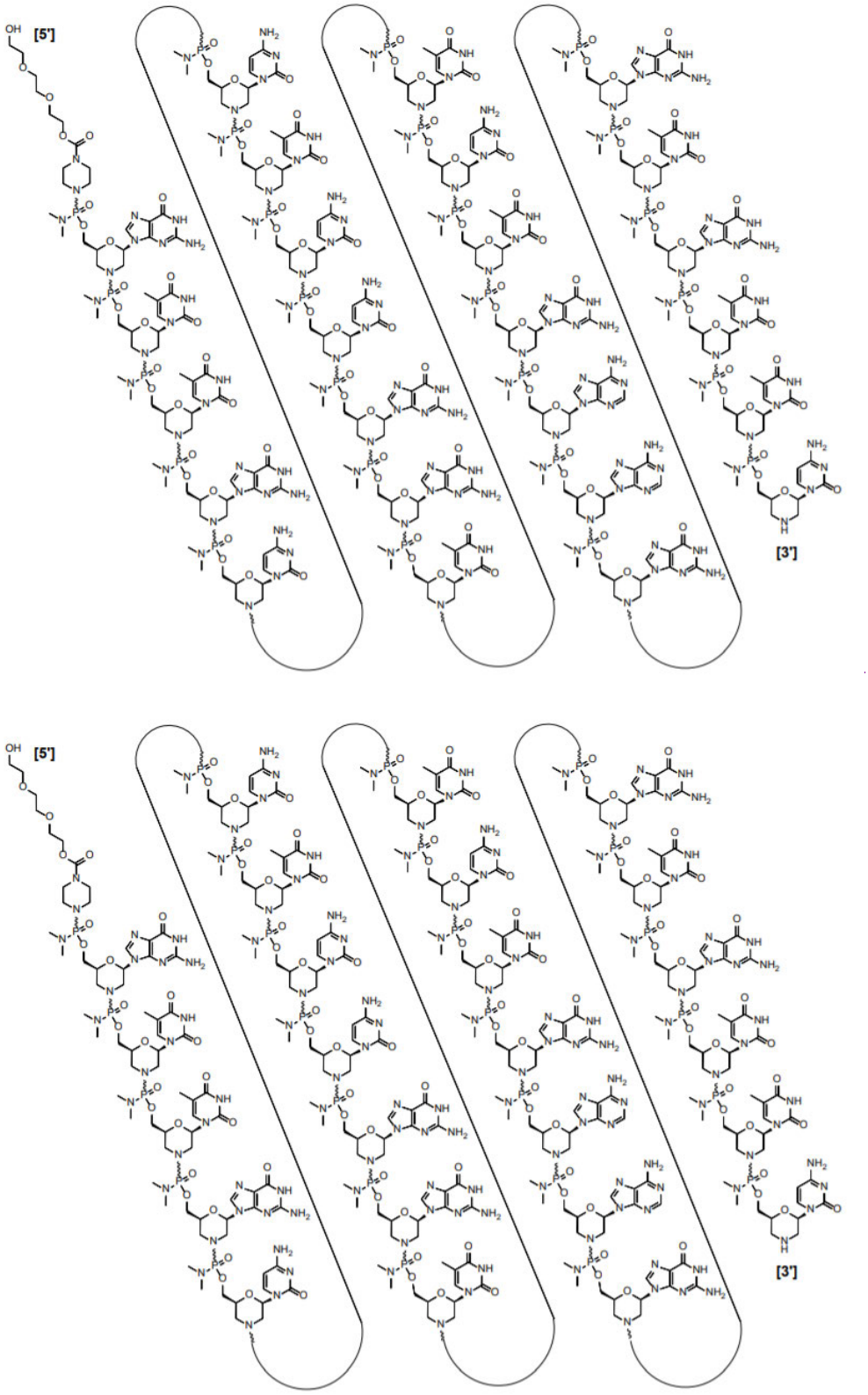
119. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

120. Sarepta admits that Paragraph 120 quotes claim 1 of the '461 patent.

121. Paragraph 121 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta denies the allegations in Paragraph 121.

122. Paragraph 122 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that the label for Vyondys 53® indicates that the structure of golodirsen is:

[redacted]



Sarepta denies any remaining allegations in Paragraph 122.

[redacted]

123. Sarepta denies the allegations in Paragraph 123.

124. Sarepta denies the allegations in Paragraph 124.

125. Sarepta denies the allegations in Paragraph 125.

126. Sarepta denies the allegations in Paragraph 126.

127. Sarepta denies the allegations in Paragraph 127.

128. Sarepta denies the allegations in Paragraph 128.

CLAIM VI
(Infringement of the '106 Patent)

129. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

130. Sarepta admits that Paragraph 130 quotes claim 1 of the '106 patent.

131. Paragraph 131 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that the label for Vyondys 53® describes the structure of golodirsen. Sarepta denies any remaining allegations in Paragraph 131.

132. Sarepta denies the allegations in Paragraph 132.

133. Sarepta denies the allegations in Paragraph 133.

134. Sarepta denies the allegations in Paragraph 134.

135. Sarepta denies the allegations in Paragraph 135.

136. Sarepta denies the allegations in Paragraph 136.

137. Sarepta denies the allegations in Paragraph 137.

CLAIM VII
(Infringement of the '741 Patent)

138. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

139. Sarepta admits that Paragraph 139 quotes claim 1 of the '741 patent.

[redacted]

140. Paragraph 140 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Paragraph 140 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019) § 1; Highlights of Prescribing Information (Feb. 11, 2021) § 1." Sarepta admits that Vyondys 53® is indicated for the treatment of DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 140.

141. Sarepta admits that Paragraph 141 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019)" and "Highlights of Prescribing Information (Feb. 11, 2021)." Sarepta admits that golodirsen is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with a genetic mutation that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 141.

142. Sarepta denies the allegations in Paragraph 142.

143. Sarepta denies the allegations in Paragraph 143.

144. Sarepta denies the allegations in Paragraph 144.

145. Sarepta denies the allegations in Paragraph 145.

CLAIM VIII
(Infringement of the '217 Patent)

146. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

147. Sarepta denies that Paragraph 147 accurately quotes the language of claim 1 of the '217 patent.

148. Paragraph 148 contains legal conclusions to which no response is required. To the extent a response is required, Sarepta admits that Vyondys 53® is indicated for the treatment of DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Sarepta denies any remaining allegations in Paragraph 148.

[redacted]

149. Sarepta admits that Paragraph 149 purports to quote in part from "Highlights of Prescribing Information (Dec. 12, 2019)" and "Highlights of Prescribing Information (Feb. 11, 2021) § 2.4." Sarepta admits that Vyondys 53® is administered via intravenous infusion. Sarepta denies any remaining allegations in Paragraph 149.

150. Sarepta denies the allegations in Paragraph 150.

151. Sarepta denies the allegations in Paragraph 151.

152. Sarepta denies the allegations in Paragraph 152.

153. Sarepta denies the allegations in Paragraph 153.

CLAIM IX
(Infringement of the '322 Patent)

154. Sarepta realleges as if fully set forth herein each of the foregoing paragraphs.

155. Sarepta denies the allegations in Paragraph 155.

156. Sarepta denies the allegations in Paragraph 156.

157. Sarepta denies the allegations in Paragraph 157.

158. Sarepta denies the allegations in Paragraph 158.

159. Sarepta denies the allegations in Paragraph 159.

160. Sarepta denies the allegations in Paragraph 160.

161. Sarepta denies the allegations in Paragraph 161.

162. Sarepta denies the allegations in Paragraph 162.

163. Sarepta denies the allegations in Paragraph 163.

164. Sarepta denies the allegations in Paragraph 164.

Sarepta denies all allegations of the SAC not specifically admitted above.

PRAYER FOR RELIEF

Sarepta denies that Nippon Shinyaku is entitled to the relief it requests or to any other relief.

[redacted]

DEMAND FOR A JURY TRIAL

Sarepta admits that Nippon Shinyaku has demanded a jury trial solely for Claims II-IX of the SAC but denies that it is entitled to one.

DEFENSES

By alleging the Defenses set forth below, Sarepta does not agree or concede that it bears the burden of proof or the burden of persuasion on any of these issues, whether in whole or in part. For its Defenses to the SAC, Sarepta alleges as follows.

First Defense
(No Breach of Contract)

Sarepta has not breached any of its contractual obligations under the MCA.

Second Defense
(The UWA Patents are Not Invalid)

All claims of the UWA Patents are not invalid or unenforceable under 35 U.S.C. § 1 *et seq.*, and Nippon Shinyaku will not be able to demonstrate otherwise by clear and convincing evidence.

Third Defense
(Non-Infringement of the NS Patents)

Sarepta has not infringed and will not infringe, directly or indirectly, any valid and enforceable claim of the NS Patents, either literally or under the doctrine of equivalents.

Fourth Defense
(Invalidity of the NS Patents)

Each asserted claim of the NS Patents is invalid for failure to comply with one or more requirements of the patent laws of the United States, including without limitation, 35 U.S.C. §§ 101, 102, 103, 112, and/or obviousness-type double patenting, and the rules, regulations, and laws pertaining thereto.

[redacted]

Fifth Defense
(Prosecution History Estoppel and Disclaimer)

Nippon Shinyaku's patent infringement claims are estopped in whole or in part by representations made or actions taken during the prosecution of the applications that matured into the NS Patents and/or related patents, under the doctrine of prosecution history estoppel and/or prosecution disclaimer.

Sixth Defense
(Failure to State a Claim)

The SAC fails to state a claim upon which relief may be granted.

Seventh Defense
(No Case or Controversy)

There is no justiciable case or controversy between the parties concerning Claims I-II of the SAC.

Eighth Defense
(Subject Matter Jurisdiction)

The Court lacks subject matter jurisdiction over Claims I-II of the SAC.

Ninth Defense
(Equitable Defenses and Remedies)

Nippon Shinyaku's breach of contract claim and/or requested remedies are barred in whole or in part under principles of equity, including unclean hands.

For example, in view of Nippon Shinyaku's knowing and repeated bad-faith breaches of the MCA as detailed in Counterclaim V below, Nippon Shinyaku has unclean hands precluding it from enforcing the MCA and depriving it of any entitlement to injunctive or other equitable relief for any alleged breach of the MCA by Sarepta.

[redacted]

Tenth Defense
(No Damages)

Nippon Shinyaku has incurred no damages as a result of the alleged patent infringement or breach of contract, which Sarepta denies.

Eleventh Defense
(No Injunctive Relief)

Nippon Shinyaku is not entitled to injunctive relief for its breach of contract claim or any other claim because it cannot succeed on the merits of any claim, any alleged injury to Nippon Shinyaku is neither immediate nor irreparable, Nippon Shinyaku has an adequate remedy at law, and the balance of the equities and the public interest are not served by the granting of an injunction. In addition, in view of Nippon Shinyaku's knowing and repeated bad-faith breaches of the MCA as detailed in Counterclaim V below, Nippon Shinyaku has unclean hands depriving it of any entitlement to injunctive or other equitable relief for any alleged breach of the MCA by Sarepta.

Twelfth Defense
(Limitation on Damages and Costs)

Nippon Shinyaku's claims for relief are barred in whole or in part, including without limitation, by 35 U.S.C. §§ 286, 287, and/or 288.

Thirteenth Defense
(No Willful Infringement)

Nippon Shinyaku is not entitled to enhanced damages pursuant to 35 U.S.C. § 284, because it cannot prove that Sarepta has willfully infringed any valid claim of the NS Patents.

Fourteenth Defense
(No Exceptional Case)

Nippon Shinyaku cannot prove that this is an exceptional case warranting an award of attorney fees under 35 U.S.C. § 285, or pursuant to the Court's inherent power.

[redacted]

Fifteenth Defense
(Unenforceability of the NS Patents due to Inequitable Conduct)

As set forth in Counterclaim VI below, the NS Patents are unenforceable due to inequitable conduct.

Reservation of Additional Defenses

Sarepta reserves any and all additional defenses available under Title 35 of the United States Code, or otherwise in law or equity, now existing, or later arising, as may be developed during discovery or supported by subsequent court rulings.

COUNTERCLAIMS

Counterclaim Plaintiffs Sarepta Therapeutics, Inc. ("Sarepta") and The University of Western Australia ("UWA") assert the following allegations and counterclaims against counterclaim Defendants Nippon Shinyaku Co., Ltd. ("Nippon Shinyaku") and NS Pharma, Inc. ("NS Pharma") (collectively "Defendants"). Sarepta and UWA reserve the right to assert additional counterclaims as warranted by facts discovered through investigation and discovery.

Nature of the Action

1. Sarepta and UWA assert counterclaims for infringement of U.S. Patent Nos. 9,994,851 ("the '851 patent") (Exhibit A); 10,227,590 ("the '590 patent") (Exhibit B); and 10,266,827 ("the '827 patent") (Exhibit C) (collectively, "the UWA Patents") arising under the patent laws of the United States, 35 U.S.C. § 1 *et seq*. These patent infringement claims arise out of Defendants' unauthorized manufacture, use, sale, offer for sale, and/or importation in the United States of Viltepso, also known as viltolarsen, and Defendants' intentional encouragement of physicians and patients to administer Viltepso.

2. Sarepta further asserts a counterclaim for declaratory judgment of invalidity of U.S. Patent Nos. 9,708,361 ("the '361 patent"); 10,385,092 ("the '092 patent"); 10,407,461 ("the '461

[redacted]

patent"); 10,487,106 ("the '106 patent"); 10,647,741 ("the '741 patent"); 10,662,217 ("the '217 patent"); and 10,683,322 ("the '322 patent") (collectively, "the NS Patents") arising under the patent laws of the United States, 35 U.S.C. § 1 *et seq.* and under the Declaratory Judgment Act, 28 U.S.C. § 2201 *et seq.*

3. Sarepta further asserts a counterclaim for breach of contract arising under Delaware state law.

4. Sarepta further asserts a counterclaim for unenforceability of the NS Patents due to inequitable conduct.

Parties

~~4.~~5. Sarepta is a corporation organized and existing under the laws of the State of Delaware with its principal place of business located at 215 First Street, Cambridge, Massachusetts 02142.

~~5.~~6. UWA is a public research university organized and existing under the laws of Australia with its main campus and offices located at 35 Stirling Highway, Crawley, Perth, Western Australia 6009. UWA is the assignee and licensor of the UWA Patents.

~~6.~~7. Nippon Shinyaku represents in its Second Amended Complaint that it is a Japanese company with a principal pace of business at 14, Nishinosho-Monguchi-cho, Kisshoin, Minami-ku, Kyoto 601-8550, Japan.

~~7.~~8. Nippon Shinyaku represents in its Second Amended Complaint that by virtue of a license agreement with NCNP, Nippon Shinyaku holds the exclusive assertion rights for the NS Patents.

~~8.~~9. Upon information and belief, NS Pharma is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at 149 East Ridgewood

[redacted]

Ave., Suite 280S, Paramus, NJ 07652. Upon information and belief, NS Pharma is a wholly owned U.S. subsidiary of Nippon Shinyaku. Upon information and belief, NS Pharma is Nippon Shinyaku's U.S. Agent authorized by the FDA to market Viltepso.

Jurisdiction and Venue

~~9.~~10. There is an actual justiciable controversy between Defendants and Sarepta and UWA concerning Defendants' liability for infringement of the UWA Patents.

~~10.~~11. Sarepta/UWA's counterclaims against Defendants for infringement of the UWA Patents arise under the patent laws of the United States, 35 U.S.C. § 1 *et seq.*

~~11.~~12. This Court has subject matter jurisdiction over the patent infringement counterclaims under 28 U.S.C. §§ 1331 and 1338(a).

~~12.~~13. There is an actual justiciable controversy between Defendants and Sarepta concerning the invalidity of the NS Patents as evidenced by Nippon Shinyaku's allegations in the Second Amended Complaint concerning Sarepta's alleged liability for infringement of the NS Patents.

~~13.~~14. Sarepta's counterclaim for declaratory judgment of invalidity of the NS Patents arises under the patent laws of the United States, 35 U.S.C. § 1 *et seq.* and under the Declaratory Judgment Act, 28 U.S.C. § 2201 *et seq.*

~~14.~~15. This Court has subject matter jurisdiction over the declaratory judgment counterclaim of invalidity of the NS Patents under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

~~15.~~16. There is an actual justiciable controversy between Nippon Shinyaku and Sarepta concerning Nippon Shinyaku's breach of contract.

~~16.~~17. Sarepta's breach of contract counterclaim arises under Delaware state law.

[redacted]

~~17.~~18. This Court has subject matter jurisdiction over the breach of contract counterclaim under 28 U.S.C. §§ 1332(a) and 1367(a).

~~18.~~19. Personal jurisdiction is proper over Nippon Shinyaku at least because Nippon Shinyaku has commenced this action and thus submitted to this Court's personal jurisdiction.

~~19.~~20. Upon information and belief, personal jurisdiction is proper over NS Pharma, a Delaware corporation, at least because it has committed acts of infringement of the UWA Patents in Delaware by offering to sell and selling Viltepso (viltolarsen) in the State of Delaware. In addition, upon information and belief, Nippon Shinyaku conferred with, and coordinated with, NS Pharma in bringing this action and thus NS Pharma has consented to this Court's personal jurisdiction.

~~20.~~21. Upon information and belief, Nippon Shinyaku directly or through its agents including its wholly owned U.S. subsidiary NS Pharma, manufactures, markets, offers to sell, sells, and/or distributes Viltepso (viltolarsen) in the State of Delaware and elsewhere in the United States, and Viltepso is prescribed by physicians practicing in Delaware and elsewhere in the United States, is available at pharmacies or medical facilities located within Delaware and elsewhere in the United States, and/or is used by patients in, and/or residents of, Delaware and elsewhere in the United States.

~~21.~~22. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391(c)(3) and 1400(b).

The UWA Patents

~~22.~~23. On June 12, 2018, the USPTO issued the '851 patent, entitled "Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof." The '851 patent is assigned to The University of Western Australia. A copy of the '851 patent is attached hereto as Exhibit A. The '851 patent is fully maintained and is valid and enforceable. Sarepta has exclusive

[redacted]

rights to the ’851 patent for the treatment of muscular dystrophies and the right to enforce the ’851 patent.

~~23.~~24. On March 12, 2019, the USPTO issued the ’590 patent, entitled “Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof.” The ’590 patent is assigned to The University of Western Australia. A copy of the ’590 patent is attached hereto as Exhibit B. The ’590 patent is fully maintained and is valid and enforceable. Sarepta has exclusive rights to the ’590 patent for the treatment of muscular dystrophies and the right to enforce the ’590 patent.

~~24.~~25. On April 23, 2019, the USPTO issued the ’827 patent, entitled “Antisense Oligonucleotides for Inducing Exon Skipping and Methods of Use Thereof.” The ’827 patent is assigned to The University of Western Australia. A copy of the ’827 patent is attached hereto as Exhibit C. The ’827 patent is fully maintained and is valid and enforceable. Sarepta has exclusive rights to the ’827 patent for the treatment of muscular dystrophies and the right to enforce the ’827 patent.

~~25.~~26. The UWA Patents are listed in the U.S. Food and Drug Administration’s (“FDA”) *Approved Drug Products with Therapeutic Equivalence Evaluations* (“the Orange Book”) for New Drug Application (“NDA”) No. 211970 for Sarepta’s Vyondys 53® product, also known as golodirsen. Each of the UWA Patents covers, *inter alia*, an antisense oligonucleotide of 20 to 31 bases wherein a base sequence comprises at least 12 consecutive bases of SEQ ID NO: 195 disclosed in the UWA Patents, in which uracil bases are thymine bases, and a method of using it for the treatment of Duchenne Muscular Dystrophy (“DMD”) in patients who have a mutation of the DMD gene that is amenable to exon 53 skipping.

[redacted]

Background

Defendants' Infringing Product

~~26.~~27. Upon information and belief, Defendants' product, Viltepso (viltolarsen), is a morpholino antisense oligonucleotide comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA. Viltepso (viltolarsen) Highlights of Prescribing Information (Aug. 2020),[3] § 11; *see also* Viltepso (viltolarsen) Highlights of Prescribing Information (Mar. 2021)[4]. Viltepso contains 21 bases and CCTCCGGTTCTGAAGGTGTTC as the base sequence. Viltepso (viltolarsen) Highlights of Prescribing Information (Mar. 2021), § 11.

~~27.~~28. Upon information and belief, Viltepso induces exon 53 skipping in a human dystrophin pre-mRNA. *Id.* § 12.1.

~~28.~~29. Upon information and belief, Viltepso is administered to DMD patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping and induces skipping of exon 53 of dystrophin pre-mRNA. *Id.* §§ 1, 12.1. Defendants' label for Viltepso has encouraged and continues to encourage such use.

~~29.~~30. Upon information and belief, Defendants conducted pre-clinical and clinical development of Viltepso (viltolarsen), including clinical trials, to generate data in support of their submission of an NDA with the FDA for Viltepso (viltolarsen).

[3] Viltepso (viltolarsen) Highlights of Prescribing Information (Rev. Aug. 2020), https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212154Orig1s000lbl.pdf (last visited Jan. 28, 2022).

[4] Viltepso (viltolarsen) Highlights of Prescribing Information (Rev. Mar. 2021), https://www.viltepso.com/prescribing-information (last visited Jan. 28, 2022).

[redacted]

~~30.~~31. Upon information and belief, on October 2, 2019, Nippon Shinyaku announced that it had submitted a rolling NDA for Viltepso (viltolarsen) with the FDA. Nippon Shinyaku News Release (Oct. 2, 2019).[5]

~~31.~~32. On August 12, 2020, the FDA announced it had granted accelerated approval to Viltepso for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. FDA News Release (Aug. 12, 2020).[6]

~~32.~~33. Upon information and belief, Nippon Shinyaku announced that NS Pharma, a wholly owned U.S. subsidiary of Nippon Shinyaku, had launched Viltepso for commercial sales in the United States as of August 19, 2020. Nippon Shinyaku News Release (Aug. 20, 2020).[7] Upon information and belief, NS Pharma is Nippon Shinyaku's U.S. Agent authorized by the FDA to market Viltepso. *Id.*

~~33.~~34. Upon information and belief, since at least August 2020, Defendants have encouraged physicians to treat DMD patients by administering Viltepso to induce skipping of exon 53 of dystrophin pre-mRNA including through their labels for Viltepso. Defendants have also facilitated pricing and reimbursement of Viltepso in the United States.

Defendants' Awareness of the UWA Patents

~~34.~~35. Upon information and belief, Defendants have been familiar with and knew of the UWA Patents prior to this litigation. Upon information and belief, Defendants believed prior to this litigation that one or more claims of the UWA Patents covered Viltepso (viltolarsen). When

[5] Nippon Shinyaku Press Release (Oct. 2, 2019), https://www.nippon-shinyaku.co.jp/file/download.php?file_id=3838 (last visited Jan. 28, 2022).

[6] FDA News Release (Aug. 12, 2020), https://www.fda.gov/news-events/press-announcements/fda-approves-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation (last visited Jan. 28, 2022).

[7] Nippon Shinyaku Press Release (Aug. 20, 2020), https://www.nippon-shinyaku.co.jp/file/download.php?file_id=3868 (last visited Jan. 28, 2022).

[redacted]

the UWA Patents issued in 2018 and 2019, for example, Defendants' NDA seeking marketing approval for viltolarsen was under regulatory review in the United States. Upon information and belief, Defendants became aware of the UWA Patents after the UWA Patents were submitted for listing in the FDA Orange Book for Vyondys 53® in December 2019. Upon information and belief, Defendants expected that their Viltepso (viltolarsen) product, if approved, would compete directly with Sarepta's Vyondys 53® (golodirsen) product. Upon information and belief, Defendants learned of the UWA Patents through their efforts to research and/or monitor third-party U.S. patents that could potentially interfere with their ability to market Viltepso (viltolarsen) in the United States.

~~35.~~36. Sarepta and Nippon Shinyaku entered into a Mutual Confidentiality Agreement ("MCA") effective June 1, 2020. Upon information and belief, Defendants were already aware of the UWA Patents when Sarepta and Nippon Shinyaku began business discussions under the MCA in June 2020.

COUNTERCLAIM I
(Infringement of the '851 Patent)

~~36.~~37. Sarepta and UWA reallege each of the foregoing Paragraphs 1-~~35~~36 as if fully set forth herein.

~~37.~~38. Sarepta and UWA incorporate by reference Sarepta's answers and responses to Nippon Shinyaku's Second Amended Complaint ("SAC") as if fully set forth herein.

~~38.~~39. Claim 1 of the '851 patent recites:

> An antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the target region is within annealing site H53A(+23+47) and annealing site H53A(+39+69), wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), in which uracil bases

[redacted]

> are thymine bases, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping; or a pharmaceutically acceptable salt thereof.

~~39.~~40. Upon information and belief, Viltepso satisfies each element of at least claim 1 of the '851 patent.

~~40.~~41. Viltolarsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. *See* Viltepso (viltolarsen) Highlights of Prescribing Information (Rev. Mar. 2021), § 11. Viltolarsen contains 21 linked subunits. *Id.* The base sequence of viltolarsen is CCTCCGGTTCTGAAGGTGTTC, which includes CTGAAGGTGTTC as 12 consecutive bases. *Id.*

~~41.~~42. Viltepso is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. *Id.* § 12.1.

~~42.~~43. Viltepso is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. *Id.* § 1.

~~43.~~44. Upon information and belief, Defendants have directly infringed and continue to directly infringe at least claim 1 of the '851 patent, either literally or under the doctrine of equivalents, by engaging in the commercial manufacture, use, offer for sale, sale, and/or importation of Viltepso in the United States in violation of 35 U.S.C. § 271(a).

~~44.~~45. Upon information and belief, Defendants knew or should have known of the existence of the '851 patent at least as of the date of its issuance. For example, upon information and belief, Defendants learned of the '851 patent through their monitoring of third-party patent rights, including the UWA Patents, and their efforts to obtain approval for, and market, viltolarsen

[redacted]

in the United States. Upon information and belief, Defendants were aware of the '851 patent before June 2020 when Nippon Shinyaku and Sarepta began business discussions under the MCA.

~~45.~~46. Viltepso is approved for use in the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. *See* Viltepso (viltolarsen) Highlights of Prescribing Information (Rev. Mar. 2021), § 1. Upon information and belief, Viltepso has no substantial non-infringing uses, and Defendants know that Viltepso is especially made or especially adapted for use in infringement of the '851 patent.

~~46.~~47. Upon information and belief, Defendants' sale, offer for sale, and/or distribution of Viltepso includes labeling indicating that it is approved by the FDA to treat DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping and instructs physicians and patients to use Viltepso to treat DMD. *Id*. Upon information and belief, Defendants specifically intend that Viltepso be used to treat DMD with the knowledge that it would infringe the '851 patent.

~~47.~~48. Upon information and belief, Defendants have induced and/or contributed to and continue to induce and/or contribute to infringement of at least claim 1 of the '851 patent, either literally or under the doctrine of equivalents, in violation of 35 U.S.C. §§ 271(b) and/or (c).

~~48.~~49. Upon information and belief, Defendants' infringement of the '851 patent has been willful and continues to be willful, entitling Sarepta and UWA to enhanced damages pursuant to 35 U.S.C. § 284. Upon information and belief, Defendants knew or should have known that their conduct related to the development, manufacture, use, offer for sale, sale, and/or importation of Viltepso constituted an unreasonable risk of infringement of at least claim 1 of the '851 patent.

~~49.~~50. This case is exceptional and Sarepta and UWA are entitled to attorneys' fees and costs incurred in prosecuting this action pursuant to 35 U.S.C. § 285.

[redacted]

COUNTERCLAIM II
(Infringement of the '590 Patent)

~~50.~~51. Sarepta and UWA reallege each of the foregoing Paragraphs 1-~~49~~50 as if fully set forth herein.

~~51.~~52. Sarepta and UWA incorporate by reference Sarepta's answers and responses to Nippon Shinyaku's Second Amended Complaint as if fully set forth herein.

~~52.~~53. Claim 1 of the '590 patent recites:

> An antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), in which uracil bases are thymine bases, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping; or a pharmaceutically acceptable salt thereof.

~~53.~~54. Upon information and belief, Viltepso satisfies each element of at least claim 1 of the '590 patent.

~~54.~~55. Viltolarsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. *See* Viltepso (viltolarsen) Highlights of Prescribing Information (Rev. Mar. 2021), § 11. Viltolarsen contains 21 linked subunits. *Id.* The base sequence of viltolarsen is CCTCCGGTTCTGAAGGTGTTC, which includes CTGAAGGTGTTC as 12 consecutive bases. *Id.*

~~55.~~56. Viltepso is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with a genetic mutation that is amenable to exon 53 skipping. *Id.* § 12.1.

~~56.~~57. Viltepso is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. *Id.* § 1.

[redacted]

~~57.~~58. Upon information and belief, Defendants have directly infringed and continue to directly infringe at least claim 1 of the '590 patent, either literally or under the doctrine of equivalents, by engaging in the commercial manufacture, use, offer for sale, sale, and/or importation of Viltepso in the United States in violation of 35 U.S.C. § 271(a).

~~58.~~59. Upon information and belief, Defendants knew or should have known of the existence of the '590 patent at least as of the date of its issuance. For example, upon information and belief, Defendants learned of the '590 patent through their monitoring of third-party patent rights, including the UWA Patents, and their efforts to obtain approval for, and market, viltolarsen in the United States. Upon information and belief, Defendants were aware of the '590 patent before June 2020 when Nippon Shinyaku and Sarepta began business discussions under the MCA.

~~59.~~60. Viltepso is approved for use in the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. *See* Viltepso (viltolarsen) Highlights of Prescribing Information (Rev. Mar. 2021), § 1. Upon information and belief, viltolarsen has no substantial non-infringing uses, and Defendants know that viltolarsen is especially made or especially adapted for use in infringement of the '590 patent.

~~60.~~61. Upon information and belief, Defendants' sale, offer for sale, and/or distribution of Viltepso includes labeling indicating that it is approved by the FDA to treat DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping and instructs physicians and patients to use Viltepso to treat DMD. *Id*. Upon information and belief, Defendants specifically intend that Viltepso be used to treat DMD with the knowledge that it would infringe the '590 patent.

[redacted]

~~61.~~62. Upon information and belief, Defendants have induced and/or contributed to and continue to induce and/or contribute to infringement of at least claim 1 of the '590 patent, either literally or under the doctrine of equivalents, in violation of 35 U.S.C. §§ 271(b) and/or (c).

~~62.~~63. Upon information and belief, Defendants' infringement of the '590 patent has been willful and continues to be willful, entitling Sarepta and UWA to enhanced damages pursuant to 35 U.S.C. § 284. Upon information and belief, Defendants knew or should have known that their conduct related to the development, manufacture, use, offer for sale, sale, and/or importation of Viltepso constituted an unreasonable risk of infringement of at least claim 1 of the '590 patent.

~~63.~~64. This case is exceptional and Sarepta and UWA are entitled to attorneys' fees and costs incurred in prosecuting this action pursuant to 35 U.S.C. § 285.

COUNTERCLAIM III
(Infringement of the '827 Patent)

~~64.~~65. Sarepta and UWA reallege each of the foregoing Paragraphs 1-~~63~~64 as if fully set forth herein.

~~65.~~66. Sarepta and UWA incorporate by reference Sarepta's answer and responses to Nippon Shinyaku's Second Amended Complaint as if fully set forth herein.

~~66.~~67. Claim 1 of the '827 patent recites:

> A method for treating a patient with Duchenne muscular dystrophy (DMD) in need thereof who has a mutation of the DMD gene that is amenable to exon 53 skipping, comprising administering to the patient an antisense oligonucleotide of 20 to 31 bases comprising a base sequence that is 100% complementary to consecutive bases of a target region of exon 53 of the human dystrophin pre-mRNA, wherein the base sequence comprises at least 12 consecutive bases of CUG AAG GUG UUC UUG UAC UUC AUC C (SEQ ID NO: 195), in which uracil bases are thymine bases, wherein the antisense oligonucleotide is a morpholino antisense oligonucleotide, and wherein the antisense oligonucleotide induces exon 53 skipping; or a pharmaceutically acceptable salt thereof.

[redacted]

~~67.~~68. Upon information and belief, the use of Viltepso satisfies each element of, and directly infringes, either literally or under the doctrine of equivalents, at least claim 1 of the '827 patent.

~~68.~~69. Viltepso is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. *See* Viltepso (viltolarsen) Highlights of Prescribing Information (Rev. Mar. 2021), § 1.

~~69.~~70. Upon information and belief, Defendants knew or should have known of the existence of the '827 patent at least as of the date of its issuance. For example, upon information and belief, Defendants learned of the '827 patent through their monitoring of third-party patent rights, including the UWA Patents, and their efforts to obtain approval for, and market, viltolarsen in the United States. Upon information and belief, Defendants were aware of the '827 patent before June 2020 when Nippon Shinyaku and Sarepta began business discussions under the MCA.

~~70.~~71. Viltepso is approved for use in the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. *Id*. Upon information and belief, viltolarsen has no substantial non-infringing uses, and Defendants know that viltolarsen is especially made or especially adapted for use in infringement of the '827 patent.

~~71.~~72. Upon information and belief, Defendants' sale, offer for sale, and/or distribution of Viltepso includes labeling indicating that it is approved by the FDA to treat DMD in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping and instructs physicians and patients to use Viltepso to treat DMD. *Id*. Upon information and belief, Defendants specifically intend that Viltepso be used to treat DMD with the knowledge that it would infringe the '827 patent.

[redacted]

~~72.~~73. Upon information and belief, Defendants have induced and/or contributed to and continue to induce and/or contribute to infringement of at least claim 1 of the '827 patent, either literally or under the doctrine of equivalents, in violation of 35 U.S.C. §§ 271(b) and/or (c).

~~73.~~74. Upon information and belief, Defendants' infringement of the '827 patent has been willful and continues to be willful, entitling Sarepta and UWA to enhanced damages pursuant to 35 U.S.C. § 284. Upon information and belief, Defendants knew or should have known that their conduct related to the development, manufacture, use, offer for sale, sale, and/or importation of Viltepso constituted an unreasonable risk of infringement of at least claim 1 of the '827 patent.

~~74.~~75. This case is exceptional and Sarepta and UWA are entitled to attorneys' fees and costs incurred in prosecuting this action pursuant to 35 U.S.C. § 285.

COUNTERCLAIM IV
(Declaration of Invalidity of the NS Patents)

~~75.~~76. Sarepta realleges each of the foregoing Paragraphs 1-~~74~~75 as if fully set forth herein.

~~76.~~77. Sarepta incorporates by reference its answers and responses to Nippon Shinyaku's Second Amended Complaint.

~~77.~~78. Each claim of the NS Patents is invalid for failure to comply with one or more requirements of the patent laws of the United States, including without limitation, 35 U.S.C. §§ 101, 102, 103, 112, and/or obviousness-type double patenting, and the rules, regulations, and laws pertaining thereto.

~~78.~~79. By way of example, the claims of the NS Patents are invalid under 35 U.S.C. §§ 102 and/or 103 in view of Popplewell, L.J., *Comparative Analysis of Antisense Oligonucleotide Sequences Targeting Exon 53 of the Human DMD Gene: Implications for Future Clinical Trials*, Neuromuscular Disorders 20:102–110 (2010) ("Popplewell") and Sazani, P., *Safety Pharmacology*

[redacted]

and Genotoxicity Evaluation of AVI-4658, Int'l J. Toxicology 29(2):143–156 (2010) ("Sazani"), alone or in combination with other prior art, for at least the reasons set forth in Sarepta's IPR Petitions challenging the NS Patents. In granting Sarepta's IPR Petitions challenging all claims of all seven NS Patents, for example, the Patent Trial and Appeal Board found Sarepta's arguments and evidence of unpatentability persuasive, concluding in each institution decision that Sarepta "has demonstrated a reasonable likelihood of success in proving that the challenged claims of the [patent] are unpatentable." *See Sarepta Therapeutics, Inc. v. Nippon Shinyaku Co., Ltd.*, Decisions Granting Institution in IPR2021-01134, Paper No. 20 (Jan. 12, 2022); IPR2021-01135, Paper No. 20 (Jan. 12, 2022); IPR2021-01136, Paper No. 19 (Jan. 13, 2022); IPR2021-01137, Paper No. 18 (Jan. 13, 2022); IPR2021-01138, Paper No. 18 (Jan. 13, 2022); IPR2021-01139, Paper No. 18 (Jan. 13, 2022); and IPR2021-01140, Paper No. 18 (Jan. 12, 2022).

~~79.~~80. An actual case or controversy exists between Sarepta and Defendants as to whether the claims of the NS Patents are invalid.

~~80.~~81. Sarepta is entitled to a declaratory judgment that the claims of the NS Patents are invalid.

~~81.~~82. This case is exceptional and Sarepta is entitled to attorneys' fees and costs incurred in prosecuting this action pursuant to 35 U.S.C. § 285.

COUNTERCLAIM V
~~(Breach of Contract)~~
(Breach of Contract)

~~82.~~83. Sarepta realleges each of the foregoing Paragraphs 1-~~81~~82 as if fully set forth herein.

~~83.~~84. Sarepta incorporates by reference its answers and responses in Sarepta's Answer and Counterclaims to Nippon Shinyaku's Second Amended Complaint as fully set forth herein.

[redacted]

~~84.~~85. Sarepta asserts a claim for breach of contract arising under Delaware state law. This Court has subject matter jurisdiction over this breach of contract claim under 28 U.S.C. §§ 1332(a) and 1367(a).

~~85.~~86. This claim for breach of contract arises out of Nippon Shinyaku's material breach of the MCA with Sarepta.

~~86.~~87. Properly interpreted, the MCA is a valid and enforceable contract between Sarepta and Nippon Shinyaku.

~~87.~~88. Sections 1-3 of the MCA define "Confidential Information" and proscribe improper disclosures or uses of confidential information beyond the permitted purposes. Section 2.2, entitled "Obligations of Confidentiality and Non-Use," states among other relevant provisions that:

> The Parties intend and agree that this Agreement, the Proposed Transaction and all disclosures, including all meetings, discussions, correspondence, communications, documents, or other materials exchanged between the Parties made in connection with this Agreement and the Proposed Transaction shall not be submitted, referenced, admitted or otherwise used by the Recipient, its Affiliates, or their respective Representatives against the other Party in any legal action, except in an action to enforce the terms of this Agreement, and shall be treated as conducted in the aid of negotiation and shall be governed by and entitled to the protections and privileges of Delaware Rule of Evidence 408 and Federal Rule of Evidence 408, as well as any and all analogous or applicable privileges or additional limitations on use and disclosure set forth herein. Furthermore, regardless of whether the Proposed Transaction leads to any arrangement or resolution of issues, the fact that these confidential Proposed Transactions occurred shall not be referenced in any legal action currently pending, including but not limited to the EP Oppositions, the JP Actions, or the Potential Actions. Neither Party nor their Affiliates or Representatives shall in any way attempt to place into evidence any document, fact, statement or opinion in any way relating to the Proposed Transaction for any purpose, regardless of whether such document, fact, statement or opinion would be admissible under FRE 408 or any other analogous or applicable privilege.

[redacted]

D.I. 2-1 at 3.

~~88.~~89. On July 14, 2021, Nippon Shinyaku filed its original Complaint in this action containing confidential information in violation of its agreement, materially breaching its obligations under the MCA, Sections 1-3.

~~89.~~90. Notwithstanding that in its first set of Rule 12 responsive motions Sarepta raised its objection to such confidential information appearing in Nippon Shinyaku's original Complaint contrary to the terms of the MCA, Nippon Shinyaku again included the same confidential material in its First Amended Complaint ("FAC"), filed September 10, 2021 (D.I. 39).

~~90.~~91. Sarepta renewed its objection in subsequent Rule 12 responsive motions (D.I. 53, 54) to such confidential information appearing in Nippon Shinyaku's FAC contrary to the terms of the MCA.

~~91.~~92. On December 20, 2021, the Court found that Nippon Shinyaku had violated the confidentiality and non-use provisions of the MCA and struck from the FAC the second sentence of paragraph 2 as well as paragraphs 11, 78, and 91 of the FAC. (Hearing Tr. at 31-34; D.I. 84.)

~~92.~~93. As the Court found, Nippon Shinyaku "agreed not to hold the parties' confidential communications against Sarepta in future litigation" because the terms of the valid and enforceable MCA had prohibitions against mentioning confidential communications in legal actions. *Id*. at 32, 34. But Nippon Shinyaku materially breached the terms of the agreement by including confidential information in its original Complaint and again in its FAC, even after being put on notice of its breach, requiring further briefing, motions practice, and a ruling by this Court striking the confidential information from Nippon Shinyaku's pleading.

[redacted]

~~93.~~94. Sarepta has suffered prejudice and injury by virtue of Nippon Shinyaku's knowing and repeated bad-faith breaches of the MCA's confidentiality and non-use provisions of Section 2, entitling Sarepta to damages in an amount exceeding $75,000.

~~94.~~95. In addition, in view of Nippon Shinyaku's knowing and repeated bad-faith breaches of the MCA, Nippon Shinyaku has unclean hands precluding enforcement of the MCA and depriving it of any entitlement to injunctive or other equitable relief for any alleged breach of the MCA by Sarepta.

COUNTERCLAIM VI
(Declaratory Judgment of Unenforceability of the NS Patents Due to Inequitable Conduct)

96. Sarepta realleges each of the foregoing Paragraphs 1-95 as if fully set forth herein.

97. As set forth below, the NS Patents are unenforceable due to inequitable conduct based on material misrepresentations and omission of material information that occurred during prosecution of the NS Patents at the USPTO. The single most reasonable inference that can be drawn from the facts discovered to date is that [redacted] intended to deceive the USPTO by: (1) mispresenting that a claimed oligomer exhibited "superior skipping activity" over a prior art oligomer [redacted] and (2) withholding the Sazani paper during prosecution of the NS Patent.

I. Background Information on the NS Patents

A. The NS Patents

98. NS has asserted seven patents against Sarepta in this litigation: U.S. Patent Nos. 9,708,361 ("the '361 patent"); 10,385,092 ("the '092 patent); 10,407,461 ("the '461 patent");

[redacted]

10,487,106 ("the '106 patent"); 10,647,741 ("the '741 patent"); 10,662,217 ("the '217 patent"); and 10,683,322 ("the '322 patent) (collectively, "the NS Patents").

99. The '361 patent stems from U.S. Application No. 14/615,504, filed February 6, 2015. The '504 application was filed as a continuation of U.S. Application No. 13/819,520, which claims priority to International Patent Application No. PCT/JP2011/070318, filed August 31, 2011 ("International PCT Application"). The International PCT Application claims priority to Japanese Application No. 2010-196032, filed September 1, 2010 ("JP Application").

100. The '520 application issued as U.S. Patent No. 9,079,934. Ex. AA, Items (10) & (21). Claim 1 of the '934 patent recites:

> 1. An antisense oligomer which causes skipping of the 53rd exon in the human dystrophin gene, consisting of the nucleotide sequence of SEQ ID NO: 35, wherein the antisense oligomer is an oligonucleotide having the sugar moiety and/or the phosphate-binding region of at least one nucleotide constituting the oligonucleotide modified, or a morpholino oligomer.

101. NS has requested a patent term extension of the '934 patent based on the approved product, VILTEPSO (viltolarsen). *See* Ex. AB. The '934 patent is not asserted against Sarepta in this litigation.

102. Claim 1 of the '361 patent recites:

> 1. An antisense oligomer which causes skipping of the 53rd exon in the human dystrophin gene, consisting of the nucleotide sequence of SEQ ID NO: 57, wherein the antisense oligomer is an oligonucleotide in which the sugar moiety and/or the phosphate-binding region of at least one nucleotide constituting the oligonucleotide is modified, or a morpholino oligomer.

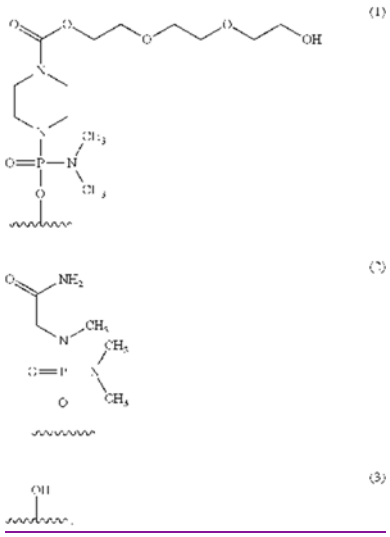
103. Claim 4, which depends from claim 1, recites:

> 4. The antisense oligomer according to claim 1, which is a morpholino oligomer.

104. Claim 6, which depends from claim 4, recites:

[redacted]

6. The antisense oligomer according to claim 4, wherein the 5' end is any one of the groups of chemical formulae (1) to (3) below:



105. Table 7 of the '361 patent indicates that SEQ ID NO: 57 corresponds to an antisense oligomer named "H53_36-60," which is intended to bind positions 36 to 60 of exon 53 of the human dystrophin pre-mRNA ("Exon 53").[8] According to Table 7, the nucleotide sequence of the H53_36-60 oligomer is 5'-GUUGCCUCCGGUUCUGAAGGUGUUC-3'. Table 7 reports the sequences of SEQ ID NOS: 49 to 123.

106. Above Table 7, the '361 patent states that "[e]xperiments were performed using the antisense oligomers of 2'-O-methoxy-phosphorothioates (2'-OMe-S-RNA) shown by SEQ ID NO: 49 to SEQ ID NO: 123." Ex. AC, 40:24-26. Below Table 7, the '361 patent further states that "[c]omplexes of various antisense oligomers (Japan Bio Services) (1 μM) for exon 53 skipping and Lipofectamine 2000 (manufactured by Invitrogen Corp.) were prepared and 200 μl was added to RD cells . . . to reach the final concentration of 100 nM." *Id.*, 42:38-43. "The results are shown in FIGS. 9 to 17." *Id.*, 43:39.

8 [redacted]

[redacted]

107. Claim 1 of the '361 patent is generally directed to antisense oligomers (e.g., morpholino oligomers also known as "PMOs") that are intended to target positions 36 to 60 of Exon 53.

108. The '092 patent stems from U.S. Application No. 16/359,213, filed March 20, 2019. It claims priority to the '361 patent, which in turn claims priority to the International PCT Application and the JP Application. Claim 1 of the '092 patent recites:

> 1. A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer that causes skipping of the 53rd exon in a human dystrophin pre-mRNA, consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in said human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, and wherein said PMO antisense oligomer hybridizes to said pre-mRNA with Watson-Crick base pairing under physiological conditions.

109. Claim 1 of the '092 patent is generally directed to PMOs that are intended to target positions 36 to 60 of Exon 53.

110. The '461 patent stems from U.S. Application No. 16/364,451, filed March 26, 2019. It claims priority to the '361 patent, which in turn claims priority to the International PCT Application and the JP Application. Claim 1 of the '461 patent recites:

> 1. A phosphorodiamidate morpholino oligomer (PMO) antisense oligomer that causes skipping of the 53rd exon in a human dystrophin pre-mRNA, consisting of a 25-mer oligomer that is 100% complementary to the target sequence 5'-GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124) of said human dystrophin pre-mRNA, wherein said PMO antisense oligomer hybridizes to said target sequence with Watson-Crick base pairing under physiological conditions, wherein each phosphorodiamidate morpholino monomer of said PMO antisense oligomer has the formula: . . . .

[redacted]

111. The target sequence 5'-GAACACCUUCAGAACCGGAGGCAAC-3' (SEQ ID NO: 124) recited in claim 1 of the '461 patent corresponds to positions 36 to 60 of exon 53 of the human dystrophin pre-mRNA.

112. Claim 1 of the '461 patent is generally directed to PMOs that are intended to target positions 36 to 60 of Exon 53.

113. The '106 patent stems from U.S. Application No. 16/369,427, filed March 29, 2019. It claims priority to the '361 patent, which in turn claims priority to the International PCT Application and the JP Application. Claim 1 of the '106 patent recites:

> 1. A phosphorodiamidate morpholino oligomer (PMO) consisting of a 25-mer antisense oligomer that is 100% complementary, according to Watson-Crick base pairing, to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, wherein each phosphorodiamidate morpholino monomer of said PMO has the formula: . . . .

114. Claim 1 of the '106 patent is generally directed to PMOs that are intended to target positions 36 to 60 of Exon 53.

115. The '741 patent stems from U.S. Application No. 16/449,537, filed June 24, 2019. It claims priority to the '361 patent, which in turn claims priority to the International PCT Application and the JP Application. Claim 1 of the '741 patent recites:

> 1. A method comprising administering to a patient with DMD an antisense phosphorodiamidate morpholino oligomer (PMO) consisting of a 25-mer oligomer that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing, and wherein skipping of the 53rd exon is induced in said patient.

[redacted]

116. Claim 1 of the '106 patent is generally directed to a method of using PMOs that are intended to target positions 36 to 60 of Exon 53.

117. The '217 patent stems from U.S. Application No. 16/712,686, filed December 12, 2019. It claims priority to the '361 patent, which in turn claims priority to the International PCT Application and the JP Application. Claim 1 of the '217 patent recites:

> 1. A method of treating a DMD patient comprising intravenously administering to said patient an oligomer comprising:
>
> a) a phosphorodiamidate morpholino oligomer (PMO) that is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing, wherein the phosphorodiamidate morpholino monomers of said PMO have the formula: . . . .

118. Claim 1 of the '217 patent is generally directed to a method of using PMOs that are intended to target positions 36 to 60 of Exon 53.

119. The '322 patent stems from U.S. Application No. 16/717,274, filed December 17, 2019. It claims priority to the '361 patent, which in turn claims priority to the International PCT Application and the JP Application. Claim 1 of the '322 patent recites:

> 1. A solid-phase method of making an oligomer comprising a phosphorodiamidate morpholino oligomer (PMO) and a group at the 5' end of said PMO, wherein said PMO is 100% complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in a human dystrophin pre-mRNA, wherein the 53rd exon in said human dystrophin pre-mRNA consists of a nucleotide sequence corresponding to SEQ ID NO: 1, wherein said PMO hybridizes to said human dystrophin pre-mRNA with Watson-Crick base pairing, wherein the phosphorodiamidate morpholino monomers of said PMO have the formula: . . . .

120. Claim 1 of the '322 patent is generally directed to a method of making PMOs that are intended to target positions 36 to 60 of Exon 53.

[redacted]

121. The claims of the NS Patents encompass PMOs that are intended to bind positions 36 to 60 of Exon 53, or methods for making or using those PMOs.

B. Differences Between the NS Patents and the JP Application

122. The International PCT Application was published as WO 2012/029986 on March 8, 2012. Ex. AD, Items (10) & (43); *see also* Ex. AE, Items (10) & (43). The specification of the International PCT Application is substantially the same as the specification of each of the NS Patents.

123. Table 7 is the only place in the text of the International PCT Application where the H53_36-60 oligomer and its corresponding nucleotide sequence (SEQ ID NO: 57) are disclosed. Figures 9, 13, 16, and 17 are the only places in the International PCT Application reporting skipping efficiencies (%) for the H53_36-60 oligomer.

124. Except for Table 7 and Figures 9, 13, 16, and 17, the International PCT Application does not disclose the H53_36-60 oligomer or its corresponding nucleotide sequence (SEQ ID NO: 57). Except for the H53_36-60 oligomer and its corresponding nucleotide sequence (SEQ ID NO: 57), the International PCT Application does not disclose any oligomer or its corresponding nucleotide sequence that is 25 bases in length and intended to target positions 36 to 60 of Exon 53.

125. The JP Application does not include Table 7 of the International PCT Application. *See generally* Ex. AG; *see also* Ex. AH. The JP Application also does not include Figures 9 through 17 of the International PCT Application. *See id.* The JP Application does not disclose any oligomer or its corresponding nucleotide sequence that is 25 bases in length and is intended to target positions 36 to 60 of Exon 53. *See id.*

[redacted]

II. NS's Patent Activities

A. Prosecution History of the NS Patents and Its European Counterpart

1. Prosecution History of the NS Patents

126. U.S. Application No. 14/615,504 ("'504 application"), which became the '361 patent, was filed on February 6, 2015. The Utility Patent Application Transmittal for filing the '504 application was signed by Mr. Zhengyu Feng. Ex. AI, NS00000478.

127. On February 6, 2015, a First Preliminary Amendment was filed with the USPTO. The First Amendment included one independent claim (claim 1), directed to "[a]n antisense oligomer . . . consisting of a nucleotide sequence complementary to any one of the sequences consisting of the 32nd to the 56th or the 36th to the 56th nucleotides from the 5' end of the 53rd exon in the human dystrophin gene." Ex. AI, NS00000578-581. Mr. Zhengyu Feng signed the First Amendment. *Id.*

128. On February 6, 2015, the signed copy of Mr. Naoki Watanabe's inventor oath was also filed. Ex. AI, NS00000564, -592-595. The copy was signed by Mr. Naoki Watanabe on November 26, 2014. *Id.* In the oath, Mr. Watanabe declared: the attached application "was made or authorized to be made by me." *Id.*

129. On the same day, an Application Data Sheet was filed, identifying each of Nippon Shinyaku Co., Ltd. and National Center of Neurology and Psychiatry as "Applicant." Ex. AI, NS00000568-575.

130. On February 9, 2015, a Second Preliminary Amendment was filed with the USPTO. The Second Amendment included one independent claim (claim 1), directed to "[a]n antisense oligomer . . . consisting of a nucleotide sequence complementary to any one of the sequences consisting of: the 31st to the 55th, the 32nd to the 53rd, the 32nd to the 56th, the 32nd to the 61st, the 33rd to the 54th, the 33rd to the 57th, the 34th to the 58th, the 35th to the 59th, the 36th to the

[redacted]

53rd, the 36th to the 55th, the 36th to the 57th, the 36th to the 60th, or the 37th to the 61st nucleotides from the 5' end of the 53rd exon in the human dystrophin gene." Ex. AI, NS00000601-605. Mr. Zhengyu Feng signed the Second Amendment. *Id.*

131. On February 9, 2015, two copies of Power of Attorney, one from Yoshiaki Shirouchi at Nippon Shinyaku Co., Ltd. and the other from Teruhiko Higuchi at National Center of Neurology and Psychiatry, were filed. Ex. AI, NS00000609-616. The transmittal letters for both copies were signed by Mr. Zhengyu Feng. *Id.*

132. On March 25, 2016, the USPTO mailed a Non-Final Office Action. Ex. AI, NS00000736-747. In it, the Examiner rejected claim 1 and other dependent claims as "being unpatentable over," *inter alia*, Popplewell et al., U.S. Patent Publication No. 2010/0168212 ("'212 publication") and Sazani et al., U.S. Patent Publication No. 2010/0130591 ("'591 publication"). The Examiner stated: "The prior art has therefore taught that the same region targeted by the instantly claimed oligomers is superior to other regions of exon 53. The prior art has taught that sequences with SEQ ID NOS: 10-12 are included in their invention. The recited SEQ ID NOS: fall squally within SEQ ID NOS: 10-12 and 24 which have been taught by Popplewell to be a 'superior' target region of exon 53." *Id.*, NS00000742. As reproduced by the Examiner, the '212 publication discloses "the sequence +30+59 (PMO-G, or h53A30/1)." *Id.*; *see also* Ex. AX, ¶[0097].

133. On July 22, 2016, a Response to Non-Final Office Action, signed by Mr. Zhengyu Feng, was filed. Ex. AI, NS00000753-763. In the Response, Applicants amended claim 1 to recite: "[a]n antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 11 and SEQ ID NO: 57, wherein the antisense oligomer is an oligonucleotide in which the sugar moiety

[redacted]

and/or the phosphate-binding region of at least one nucleotide constituting the oligonucleotide is modified, or a morpholino oligomer." *Id*., NS00000756.

134. In the Response, Applicants stated: "the presently recited oligomers (consisting of the nucleotide sequence of SEQ ID NO: 11 and 57) offer superior skipping effects over the oligomers taught in" the '212 publication and the '591 publication. Ex. AI, NS00000761. Applicants further stated: "the recited oligomers consisting of the nucleotide sequence of SEQ ID NO: 57 also have superior skipping activity over exemplary oligomers taught in" those publications. *Id.*

135. On October 27, 2016, the USPTO mailed a Final Office Action. Ex. AI, NS00000772-784. The Examiner maintained the rejection over the '212 publication and the '591 publication. *Id*. The Examiner reiterated: "The prior art has therefore taught that the same region targeted by the instantly claimed oligomers is superior to other regions of exon 53. The prior art has taught that sequences with SEQ ID NOS:10-12 are included in their invention. The recited SEQ ID NOS: fall squarely within SEQ ID NOS:10-12 and 24 which has been taught by Popplewell to be a 'superior' target region of exon 53." *Id*., NS00000782.

136. On February 27, 2017, a Response to Final Office Action, signed by Mr. Zhengyu Feng, was filed. In the Response, Applicants amended claim 1 to recite: "[a]n antisense oligomer . . . consisting of the nucleotide sequence of SEQ ID NO: 57, wherein the antisense oligomer is an oligonucleotide in which the sugar moiety and/or the phosphate-binding region of at least one nucleotide constituting the oligonucleotide is modified, or a morpholino oligomer." *Id*., NS00000788.

137. In the Response, Applicants stated: "Figures 2-4 of the Specification . . . show that PMO No. 3 (having the nucleotide sequence of SEQ ID NO: 11; *see* Table 2) outperformed

[redacted]

exemplary antisense oligomers taught in Popplewell (PMO Nos. 12 and 15). As shown in TABLE 2, PMO Nos. 12 and 15 corresponds to the top performer taught in Popplewell (targeting sequence 30-59 of exon 53). . . . Figures 16-17 . . . show that the oligomer having the nucleotide sequence of SEQ ID NO: 57 (H53_36-60) displays a higher level skipping activity [than] that having the nucleotide sequence of SEQ ID NO: 11 (H53_32-56)." *Id.*, NS00000793.

138. Applicants also stated: "the recited oligomers consisting of the nucleotide sequence of SEQ ID NO: 57 also have superior skipping activity over exemplary oligomers taught in" those publications, "particularly the top performer taught in Popplewell." *Id.* Applicants further stated: "this superiority is unexpected, at least because none of the cited references teach or suggest such an effect." *Id.*

139. On June 12, 2017, the USPTO mailed a Notice of Allowance. Ex. AI, NS00000803-808. On July 18, 2017, the '504 application issued as the '361 patent. *Id.*, NS00000825.

140. Each of the '092, '461, '106, '741, '217, and '322 patents issued after the '361 patent issued. During prosecution of each of the '092, '461, '106, '741, '217, and '322 patents, the USPTO did not raise any rejection under 35 U.S.C. § 102. The USPTO also did not raise any rejection under 35 U.S.C. § 103 before the issuance of each of the '092, '461, '106, '741, '217, and '322 patents.

2. Prosecution History of EP3018211

141. European Patent No. 3018211 ("EP '211 Patent") is a divisional of European Patent No. 2612917 ("EP '917 Patent"). Ex. AO, Item (62). The EP '917 Patent claims priority to the International PCT Application, which in turn claims priority to the JP Application. Ex. AN, Items (86) & (30). As such, the EP '211 Patent shares a priority claim to the International PCT Application with the NS Patents.

[redacted]

142. Claim 1 of the EP '211 Patent recites:

> An antisense oligomer which causes skipping of the 53rd exon in the human dystrophin gene, consisting of a nucleotide sequence complementary to the 36th to the 60th nucleotides from the 5' end of the 53rd exon in the human dystrophin gene.

143. Claim 1 of the EP '211 Patent is generally directed to antisense oligomers (e.g., PMOs) that are intended to target positions 36 to 60 of Exon 53. As such, the claims of the EP '211 Patent share common features with the claims of the NS Patents, i.e., both sets of claims encompass PMOs that are intended to target positions 36 to 60 of Exon 53.

144. The EP '211 Patent stems from European Application No. 15199455.5, filed December 11, 2015. Ex. AP, SRPT-VYDS-0223778-83. It was filed with one independent claim (claim 1), which recited: "[a]n antisense oligomer . . . consisting of a nucleotide sequence complementary to any one of the sequences consisting of: the 31st to the 55th, the 32nd to the 53rd, the 32nd to the 61st, the 33rd to the 54th, the 33rd to the 57th, the 34th to the 58th, the 35th to the 59th, the 36th to the 53rd, the 36th to the 55th, the 36th to the 57th, the 36th to the 60th, or the 37th to the 61st nucleotides from the 5' end of the 53rd exon in the human dystrophin gene." *Id.*, SRPT-VYDS-0225739.

145. On March 16, 2016, the European Patent Office issued a European Search Opinion. *Id.*, SRPT-VYDS-0225507-08. The Examiner cited Popplewell, L.J., *Comparative Analysis of Antisense Oligonucleotide Sequences Targeting Exon 53 of the Human DMD Gene: Implications for Future Clinical Trials*, Neuromuscular Disorders 20:102–110 (2010) ("Popplewell paper") as "D1." *Id.* The Examiner stated: "The H53A30/1 variant is considered the closest and has extensive overlap with the claimed sequences. . . . The technical effect of this difference is unknown as comparative data is not present for all claimed sequences." *Id.* The "H53A30/1 variant" in the Popplewell paper corresponds to PMO-G. Ex. AW, Table 1(a).

[redacted]

146. On November 10, 2016, a Response to the European Search Opinion was filed. In the Response, claim 1 was amended to recite: "[a]n antisense oligomer . . . consisting of a nucleotide sequence complementary to the 36th to the 60th nucleotides from 5' end of the 53rd exon in the human dystrophin gene." Ex. AP, SRPT-VYDS-02262032. In the Response, Applicants explained that Table 2 of the specification discloses PMO Nos. 12 and 15, each of which "corresponds to H53A30/1 as disclosed in" the Popplewell paper. *Id.*, SRPT-VYDS-0226292-93. Applicants further stated: "In Figures 2 and 3 of the present application it is shown that SEQ ID NO: 11 corresponding to H53_32-56 (SEQ ID NO: 11) corresponding to PMO No. 3 has a higher activity than the oligomer disclosed by Popplewell et al. Furthermore, H53_36-60 (SEQ ID NO: 57) has a higher skipping activity than H53_32-56 (SEQ ID NO: 11) as shown in Figures 16 and 17. From the above explanations it is clear that H53_36-60 (SEQ ID NO: 57) has higher skipping activities than the best oligomer disclosed by Popplewell et al." *Id.* The substance of this argument is identical to that of the "superiority" arguments that Nippon Shinyaku advanced during prosecution of the '361 patent in front of the USPTO. *See supra* ¶¶126-40.

147. On February 9, 2017, the Examining Division issued a Communication, stating that in the Examiner's view, "[t]he H53A30/2," which is designated as PMO-H in the Popplewell paper, "is considered the closest in sequence and comprises the claimed smaller oligonucleotide." Ex. AP, SRPT-VYDS-0223945-946; Ex. AW, Table 1(a). On September 8, 2017, the Examining Division also requested "supportive data showing an improved activity." Ex. AP, SRPT-VYDS-0225851-82.

148. On March 16, 2018, a Response to the Communication was filed. The Response also included an "Experimental Report," in which three oligomers, "H53_36-60," "H53_33-62,"

[redacted]

and "H53_36-56," were evaluated. *Id.*, SRPT-VYDS-0224892-83; Ex. BQ. An excerpt from the Experimental Report is provided below:

> **H53_36-60:** 5′- GTTGCCTCCGGTTCTGAAGGTGTTC -3′; corresponding to SEQ ID NO: 57 of the present application, and complementary to the 36th to the 60th nucleotides from the 5′ end of the human dystrophin gene's 53rd exon; and
> **H53_33-62:** 5′- CTGTTGCCTCCGGTTCTGAAGGTGTTCTTG-3′; corresponding to H53A30/2 of D1, and complementary to the 33rd to the 62nd nucleotides from the 5′- end of the human dystrophin gene's 53rd exon.
> **H53_36-56:** 5′- CCTCCGGTTCTGAAGGTGTTC -3′; corresponding to SEQ ID NO: 35 of the present application, and complementary to the 36th to the 56th nucleotides from the 5′ end of the human dystrophin gene's 53rd exon; and
>
> The skipping efficiencies of H53_36-60 and H53_33-62 were measured in separate *in vitro* experiments but both experiments included H53_36-56 as control. Briefly, 10 μM of

149. The Experimental Report further provides results from Experiment 1 and Experiment 2 as shown below (Ex. BQ, 2):

(2) Results

Experiment 1

Sequences	Concentration (μM)	Repeat number	Skipping efficiency(%)	
			Mean	Standard deviation
H53_36-60	10	3	45.5	10.9
H53_36-56	10	3	68.0	1.9

Experiment 2

Sequences	Concentration (μM)	Repeat number	Skipping efficiency(%)	
			Mean	Standard deviation
H53_33-62	10	3	32.7	4.5
H53_36-56	10	3	76.2	8.0

150. Based on these results, the Experimental Report concluded: "H53_36-60 showed higher skipping efficiency in experiment 1 than H53_33-62 did in experiment 2, although control sequence of H53_36-56 showed lower skipping efficiency in test 1 than in test 2. Thus, the presently claimed oligomer H53_36-60 has superior skipping activity over H53A30/2" i.e., PMO-H in the Popplewell paper. *Id.*

[redacted]

151. On April 12, 2018, the Examining Division issued a Communication noting that "[t]he claims are allowable." Ex. AP, SRTP-VYDS-0225280. On July 11, 2019, the Examining Division issued a Decision to grant a European Patent. *Id.*, SRPT-VYDS-0223991-93. On August 19, 2019, the Certificate for a European patent was transmitted. *Id.*, SRPT-VYDS-0226522.

152. On May 6, 2020, Sarepta filed a Notice of Opposition, requesting the revocation of EP '211 Patent. Id., SRPT-VYDS-0225302-326. On May 7, 2020, James Poole Limited also filed a Notice of Opposition, requesting the revocation of the EP '211 Patent. *Id.*, SRPT-VYDS-0223972-989.

153. On October 27, 2020, Nippon Shinyaku submitted the "Declaration of Toshihiro Ueda," signed by Mr. Toshihiro Ueda on September 29, 2020 ("Mr. Ueda's declaration"), in the EP '211 Patent. Ex. BQ, 3 (D15). Mr. Ueda declared: "I am the person that supervised and was responsible for the experiments in the 'Experimental Report' that was filed during the examination phase of" the EP '211 Patent on March 16, 2018 ("Mr. Ueda's Experimental Report" hereafter). *Id.*

154. On January 21, 2022, NS filed a Request for Revocation of Patent, declaring that "[t]he Patent Proprietor no longer approves of the text in which the above-mentioned patent was granted and will not submit an amended text." Ex. AP, SRPT-VYDS-0226797. On January 31, 2022, the European Patent Office issued a Decision revoking the EP '211 Patent. *Id.*, SRPT-VYDS-0226351-52.

155. A copy of Mr. Ueda's Experimental Report was submitted to the USPTO on July 6, 2021 during prosecution of U.S. Application No. 17/126,366, which claims priority to, *inter alia*, the '361 patent and the International PCT Application. Ex. AM, 1; *id.*, 8 (Cite No. AC:

[redacted]

"Experimental Report submitted March 16, 2018 in EP 3018211"). The transmittal letter for submission was signed by Mr. Zhengyu Feng. *Id.*, 13.

156. A copy of Mr. Ueda's declaration was submitted to the USPTO on February 21, 2021 during prosecution of U.S. Application No. 17/175,276, which claims priority to, *inter alia*, the '361 patent and the International PCT Application. Ex. AL, Item (63); Ex. AK, 25 (Cite No. ER: "Declaration by Toshihiro Ueda submitted in Opposition Proceeding of EP 3018211, dated September 29, 2020, submitted October 27, 2020"). The transmittal letter for submission was signed by Mr. Zhengyu Feng. Ex. AK, 28. The '276 application issued as U.S. Patent No. 11,028,122 on June 8, 2021. Ex. AL, Item (45).

3. Prosecution History of JP6193343

157. Japanese Patent No. 6193343 ("JP '343 Patent") shares a priority claim with the NS Patents. *See* Ex. AQ, Item (62). Like the NS Patents, claim 1 of the JP '343 Patent also encompasses oligomers targeting positions 36 to 60 of Exon 53[9]:

> An antisense oligomer that enables skipping of the 53rd exon of the human dystrophin gene, which is complementary to a sequence consisting of nucleotides 36 to 60 from the 5' end of the 53rd exon of the human dystrophin gene.

158. Before this patent issued, the last response to office action was submitted by Hiroshi Kobayashi (representative patent attorney) on March 9, 2017. Ex. AR, 1; *see also id.*, 7. Hiroshi Kobayashi is an attorney at a law firm known as Abe, Ikubo, and Katayama ("AIK"). The response advanced arguments similar to those presented at the USPTO. Specifically, the response stated that "it is shown that PMO-G (the 30-59th) has the highest activity" in a cited prior art reference. Ex. AR, 3; *see also id.*, 9. Comparing Figures 3 and 16 of the specification, the response further

[9] Machine translated.

[redacted]

stated that "it turns out that oligomer of the present invention is highly active than PMO-G" of the cited prior art reference. Ex. AR, 5; *see also id*., 11. On July 11, 2017, the Japanese Patent Office issued a Decision to Grant. Ex. AR, 13-15; *see also id*., 16-17.

159. The response filed on March 9, 2017 omitted [redacted]

B. NS's Opposition of EP2206781

160. European Patent No. 2206781 ("EP '781 Patent") is a divisional of European Patent No. 1766010 ("EP '010 Patent"). Ex. AT, Item (62). EP '010 Patent claims priority to International Patent Application No. PCT/AU2005/000943, which published as International Patent Publication No. WO 2006/000057. Ex. AS, Items (86) & (87). The EP '781 Patent shares a priority claim with the UWA Patents, which also claim priority to International Patent Application No. PCT/AU2005/000943. *See* D.I. 89-1, Exhibits A-C, Item (63).

161. Claim 1 of EP '781 Patent recites:

> An isolated antisense oligonucleotide that binds to human dystrophin pre-mRNA wherein said oligonucleotide is 20 to 31 nucleotides in length and is an oligonucleotide that is specifically hybridizable to an exon 53 target region of the Dystrophin gene designated as annealing site H53A (+23+47), annealing site H53A (+39+69), or both,
>
> wherein said antisense oligonucleotide is a morpholino antisense oligonucleotide, and,
>
> wherein said oligonucleotide induces exon 53 skipping.

162. On August 25, 2016, NS filed a Notice of Opposition, asserting, *inter alia*, that "the alleged superior activity as argued by the patentee in the examination stage is not obtainable over the whole scope of the claim." Ex. AU, 14. NS also submitted D8 as support. *Id*.

163. D8 is an "Experimental Report" [redacted] ("Mr. Watanabe's First Declaration"). Ex. BN; [redacted]. Mr. Watanabe signed this

[redacted]

Experimental Report on August 15, 2016, attesting that "the experiments have been performed under my supervision." Ex. BN, 3. In his First Declaration, Mr. Watanabe tested three PMOs, as summarized in Table 1 of the Experimental Report and reproduced as below (*id*., 1):

Table 1

Target sequence in exon 53	Complementary nucleotide sequence	SEQ ID NO:
45–62	5'-CTGTTGCCTCCGGTTCTG-3'	SEQ ID NO: 1
49–69	5'-CATTCAACTGTTGCCTCCGGT-3'	SEQ ID NO: 2
50–69	5'-CATTCAACTGTTGCCTCCGG-3'	SEQ ID NO: 3

164. In Mr. Watanabe's First Declaration, he provides the following results from the three tested PMOs (*id*, 3):

Skipping efficiency

Concentration (μM)		3	10	30
SEQ ID NO: 1	45-62	0.2 ± 0.3	5.9 ± 1.3	15.1 ± 10.9
SEQ ID NO: 2	49-69	0.6 ± 0.3	2.0 ± 0.5	5.5 ± 2.0
SEQ ID NO: 3	50-69	1.4 ± 1.1	3.0 ± 3.4	7.1 ± 3.0

mean ± S.D.

165. Based on these results, Mr. Watanabe concluded: "Since the activity of the various oligonucleotides differs substantially it is evident that the invention cannot be worked successfully over the whole scope of the claim." *Id*, 3.

166. On September 29, 2017, NS submitted a response to the summons to attend oral proceedings. Ex. AU, 16-33. With its response, NS also submitted D8-1, "an amended version of D8." *Id*., 30.

167. D8-1 is an "Experimental Report" [redacted] ("Mr. Watanabe's Second Declaration"). Ex. BO; [redacted] Mr. Watanabe signed this Experimental Report on September 26, 2017, attesting that "the experiments have been

[redacted]

performed under my supervision." Ex. BO, 4. In his Second Declaration, Mr. Watanabe tested four PMOs, as summarized in Table 1 of the Experimental Report and reproduced as below (*id.*, 1):

Table 1

Target sequence in exon 53	Complementary nucleotide sequence	SEQ ID NOs:
45–62	5'-CTGTTGCCTCCGGTTCTG-3'	SEQ ID NO: 1
49–69	5'-CATTCAACTGTTGCCTCCGGT-3'	SEQ ID NO: 2
50–69	5'-CATTCAACTGTTGCCTCCGG-3'	SEQ ID NO: 3
39-69	5'-CATTCAACTGTTGCCTCCGGTTCTGAAGGTG-3'	SEQ ID NO: 4

168. In Mr. Watanabe's Second Declaration, he provides the following results from the four tested PMOs (Ex. BO, 3):

% Skipping efficiency

Concentration (μM)		10	30
SEQ ID NO: 1	45-62	5.9 ± 1.3	15.1 ± 10.9
SEQ ID NO: 2	49-69	2.0 ± 0.5	5.5 ± 2.0
SEQ ID NO: 3	50-69	3.0 ± 3.4	7.1 ± 3.0
SEQ ID NO: 4	39-69	18.3 ± 3.6	24.7 ± 4.4

mean ± S.D.

169. Based on these results, Mr. Watanabe concluded: "Since the activity of the various oligonucleotides differs substantially it is evident that the invention cannot be worked successfully over the whole scope of the claim." *Id.*

170. On September 29, 2017 when NS submitted a response to the summons to attend oral proceedings, NS also submitted D13, "another experimental report." Ex. AU, 31. D13 is an "Experimental Report" from Mr. Toshihiro Tone ("Mr. Tone's Declaration"). Ex. BQ. In D13, Mr. Tone attests that "the experiments have been performed under my supervision." *Id.*, 3. In D13, Mr. Tone stated that he tested the following PMOs (*id.*, 1):

[redacted]

Table 1

Target sequence in exon 53	Complementary nucleotide sequence	SEQ ID NOs.
45–62	5'-CTGTTGCCTCCGGTTCTG-3'	SEQ ID NO: 1
39-69	5'-CATTCAACTGTTGCCTCCGGTTCTGAAGGTG-3'	SEQ ID NO: 4
48-69	5'-CATTCAACTGTTGCCTCCGGTT-3'	SEQ ID NO: 5
47-68	5'-ATTCAACTGTTGCCTCCGGTTC-3'	SEQ ID NO: 6
48-68	5'-ATTCAACTGTTGCCTCCGGTT-3'	SEQ ID NO: 7
47-67	5'-TTCAACTGTTGCCTCCGGTTC-3'	SEQ ID NO: 8
49-68	5'-ATTCAACTGTTGCCTCCGGT-3'	SEQ ID NO: 9
48-67	5'-TTCAACTGTTGCCTCCGGTT-3'	SEQ ID NO: 10

171. Copies of Mr. Watanabe's First and Second Declarations (D8 & D8-1) were submitted to the USPTO during prosecution of each of the '092, '461, '106, '741, '217, and '322 patents. The transmittal letter for submission in each of these patents was signed by Mr. Zhengyu Feng. *E.g.*, Ex. AJ, NS00001125 (Cite No CS: "Experimental report submitted EPO Opposition in EP 2206781, Aug. 25, 2016"; Cite No. CT: "Experimental report (D 8-1) submitted in EPO Opposition in EP 2206781, Sept. 29, 2017"), NS00001130.

172. A copy of Mr. Tone's Declaration (D13) was also submitted to the USPTO during prosecution of each of the '092, '461, '106, '741, '217, and '322 patents. The transmittal letter for submission in each of these patents was signed by Mr. Zhengyu Feng. *E.g.*, Ex. AJ, NS00001126 (Cite No. CY: "Experimental report (D13), submitted in EPO Opposition in EP 2206781, Sept. 29, 2017"), NS00001130.

III. Mr. Naoki Watanabe

A. Mr. Watanabe's Involvement in Drafting and Prosecuting the NS Patents

173. Mr. Watanabe, referenced above, is one of the four named inventors of the NS Patents. [redacted] The other three named inventors are Youhei Satou, Shin'ichi Takeda, and Tetsuya Nagata. *See*, *e.g.*, Ex. AC, Item (72). As a named inventor

[redacted]

of the NS Patents, [redacted]

174. [redacted]

175. [redacted]

176. Item (74) of the International PCT Application identifies Hiroshi Kobayashi et al., at AIK as "Agent." Ex. AD, Item (74); *see also* Ex. AE, Item (74). The Request Form filed with the International PCT Application also identifies Eiji Katayama, Norio Ohmori, Takayuki Imazato, and Yasuhito Suzuki as additional agents with the same address as the first named agent. Ex. AF, 4.

177. [redacted]

178. [redacted]

[redacted]

¶¶175-76. AIK and its attorneys prosecuted and obtained JP '343 Patent, directed to oligomers targeting positions 36 to 60 of Exon 53. *See supra* ¶¶157-59. [redacted] intermediary between (1) Mr. Watanabe and legal professionals at NS and (2) Mr. Zhengyu Feng who acted as the undersigned representative communicating with the USPTO regarding the NS Patents.

B. Mr. Watanabe's Knowledge Regarding the State of the Art

1. The Sazani Paper

179. [redacted]

180. [redacted]

181. [redacted]

[redacted]

182. [redacted] One such publication was the Sazani paper, which reported the safety and genotoxicity of AVI-4658, as well as its chemical structure. [redacted]

183. The Sazani paper was published online on January 28, 2010. [redacted]

184. [redacted]

185. The Sazani paper reports the safety and genotoxicity of AVI-4658 evaluated in non-human primates. Ex. BM, NS00085391. As reproduced below (*id.*, NS00085393), the Sazani paper also discloses the chemical structure of AVI-4658, including its 5'-end modification. The 5'-end modification of AVI-4658, as reported in the Sazani paper, is identical to the 5'-end modification (3) recited in several claims of the NS Patents. *E.g.*, *see* ¶¶102-104, *supra*.

[redacted]

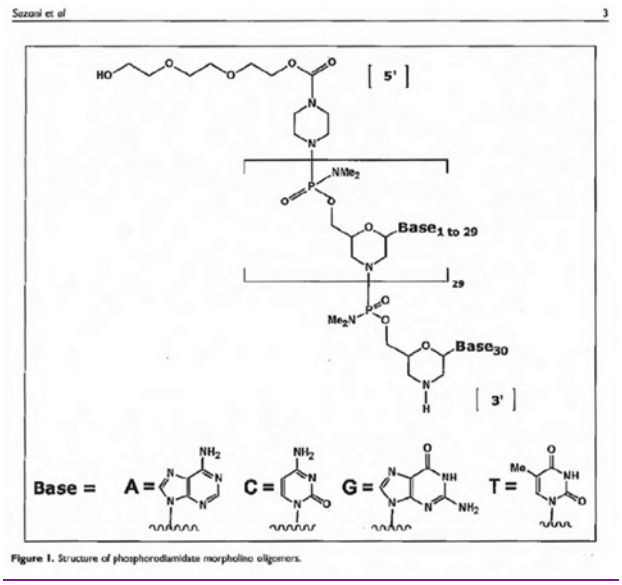


Figure 1. Structure of phosphorodiamidate morpholino oligomers.

186. [redacted] The Sazani paper was not submitted to the USPTO during prosecution of the NS Patents. Upon information and belief, the Examiner of the NS Patents was never informed about the existence of the Sazani paper during prosecution of the NS Patents.

2. The Popplewell Paper

187. [redacted]

[redacted]

[redacted]

188. [redacted]

189. PMO-A in the Popplewell paper targets positions 35 to 59 of Exon 53. [redacted] Ex. AW, Table 1(a). [redacted]

C. Mr. Watanabe's Experimental Data

1. Figures 9-17 of the NS Patents

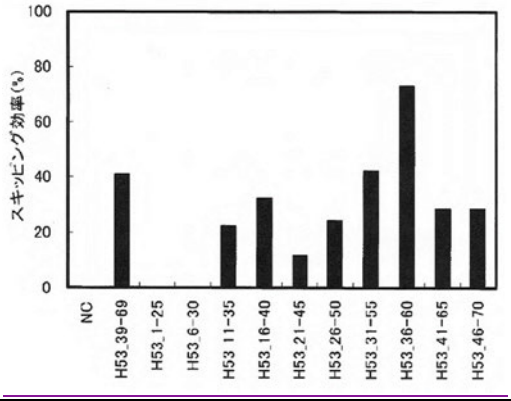
190. [redacted]

[redacted]

191. Figures 9-17 of the NS Patents report skipping efficiencies (%) of oligomers at a single concentration, 100 nM. *See* Ex. AD, Figures 9-17; *supra* ¶¶105-106. [redacted]

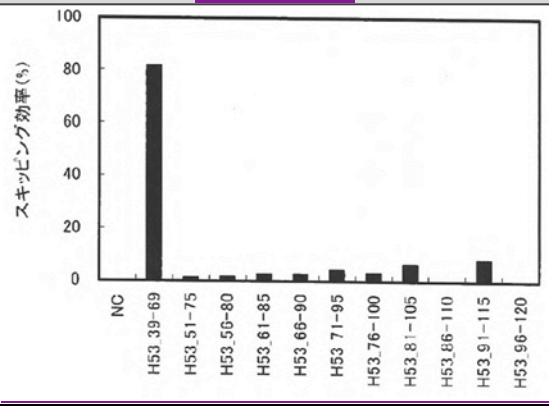
192. [redacted]

193. Figure 9 of the International PCT Application [redacted] are reproduced below [redacted]

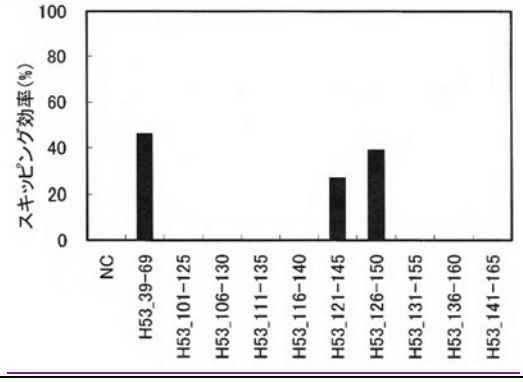
[redacted]	**Figure 9 in the International PCT Application**
[redacted]	

194. Figure 10 of the International PCT Application [redacted] are reproduced below [redacted]

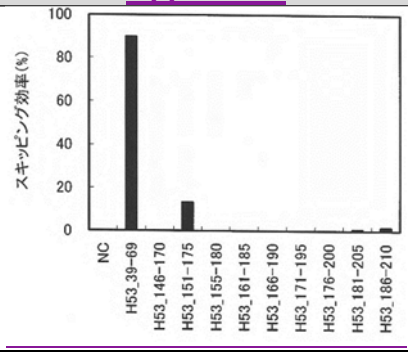
[redacted]

[redacted]	Figure 10 in the International PCT Application
[redacted]	

195. Figure 11 of the International PCT Application [redacted] are reproduced below [redacted]

[redacted]	Figure 11 in the International PCT Application
[redacted]	

196. Figure 12 of the International PCT Application [redacted] are reproduced below [redacted]

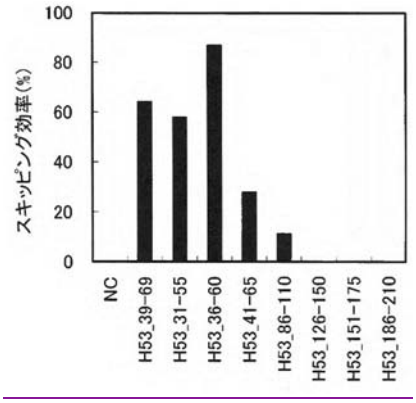
[redacted]	Figure 12 in the International PCT Application
[redacted]	

[redacted]

197. [redacted]

[redacted]

[redacted] Figure 13 of the International PCT Application [redacted] are reproduced below [redacted]

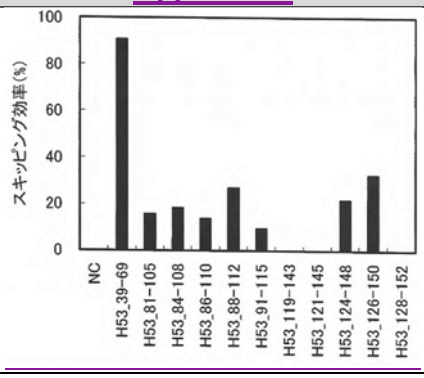
[redacted]	**Figure 13 in the International PCT Application**
[redacted]	

198. [redacted]

[redacted]

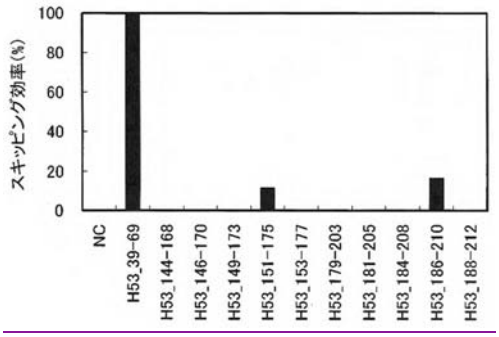
[redacted] Figure 14 of the International PCT Application [redacted] are reproduced below [redacted]

[redacted]

[redacted]	Figure 14 in the International PCT Application
[redacted]	

199. [redacted]

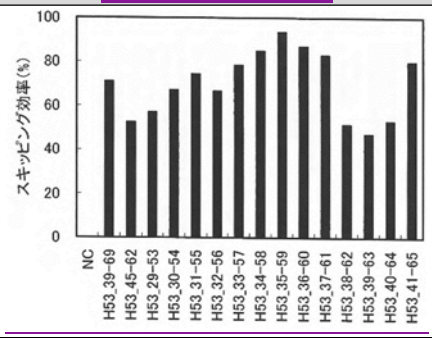
[redacted]. Figure 15 of the International PCT Application [redacted] are reproduced below [redacted]

[redacted]	Figure 15 in the International PCT Application
[redacted]	

200. [redacted]

[redacted]

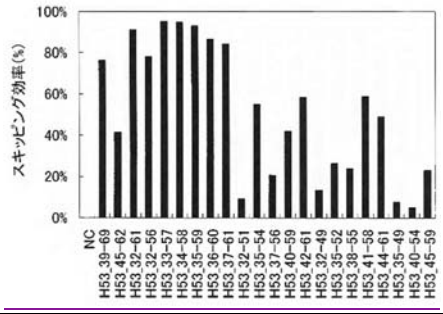
[redacted] Figure 16 of the International PCT Application [redacted] reproduced below [redacted]

[redacted]	**Figure 16 in the International PCT Application**
[redacted]	

201. [redacted]

202. [redacted] Figure 17 of the International PCT Application [redacted] are reproduced below [redacted]

[redacted]

[redacted]	Figure 17 in the International PCT Application
[redacted]	

203. [redacted]

204. [redacted] not submitted to the USPTO during prosecution of the NS Patents. Upon information and belief, the Examiner of the NS Patents was never informed [redacted] during prosecution of the NS Patents.

[redacted]

2. Mr. Ueda's Experimental Report

205. Mr. Ueda's Experimental Report was submitted to the European Patent Office on March 16, 2018, during prosecution of EP '211 Patent. *See supra* ¶¶141-56. Mr. Ueda's Experimental Report included two experiments, labeled as Experiment 1 and Experiment 2. *See supra* ¶¶148-50.

206. [redacted] Experiments 1 and 2 from Mr. Ueda's Experimental Report (Ex. BQ) [redacted] are reproduced below:

[redacted]	**Mr. Ueda's Experimental Report (Ex. BQ)**
[redacted]	Experiment 1 Sequences | Concentration (μM) | Repeat number | Skipping efficiency(%) (Mean | Standard deviation) H53_36-60 | 10 | 3 | 45.5 | 10.9 H53_36-56 | 10 | 3 | 68.0 | 1.9

[redacted]

[redacted]	Mr. Ueda's Experimental Report (Ex. BQ)
[redacted]	Experiment 2 Sequences | Concentration (μM) | Repeat number | Skipping efficiency(%) Mean | Skipping efficiency(%) Standard deviation H53_33-62 | 10 | 3 | 32.7 | 4.5 H53_36-56 | 10 | 3 | 76.2 | 8.0

207. [redacted] *with* Ex. BQ, 2. [redacted] representations made by Mr. Feng to the USPTO, [redacted] The H53_30-59 oligomer targets the same positions within Exon 53 as PMO-G from the Popplewell paper. *See* Ex. AW, Table 1(a). The H53_36-60 oligomer targets the same positions within Exon 53 as PMOs claimed by the NS Patents. *See supra* ¶¶102-121. [redacted]

208. [redacted] was not submitted to the USPTO during prosecution of the NS Patents. Upon information and belief, the

[redacted]

Examiner of the NS Patents was never informed [redacted] Upon information and belief, the Examiner of the NS Patents was never informed [redacted]

3. Mr. Watanabe's and Mr. Tone's Declarations

209. Mr. Watanabe's First and Second Declarations were submitted to the European Patent Office on August 25, 2016 and September 29, 2017, respectively, during opposition of the EP '781 Patent. *See supra* ¶¶160-72. Collectively, Mr. Watanabe's First and Second Declarations included data obtained from four PMOs targeting positions 45 to 62, 49 to 69, 50 to 69, and 39 to 69 of Exon 53, respectively. *See supra* ¶¶163-69.

210. [redacted] The experiment reported in Mr. Watanabe's Second Declaration (Ex. BO) [redacted] are reproduced below:

[redacted]	**Mr. Watanabe's Second Declaration (Ex. BO)**
[redacted]	% Skipping efficiency Concentration (μM) | 10 | 30 SEQ ID NO: 1 | 45-62 | 5.9 ± 1.3 | 15.1 ± 10.9 SEQ ID NO: 2 | 49-69 | 2.0 ± 0.5 | 5.5 ± 2.0 SEQ ID NO: 3 | 50-69 | 3.0 ± 3.4 | 7.1 ± 3.0 SEQ ID NO: 4 | 39-69 | 18.3 ± 3.6 | 24.7 ± 4.4 mean ± S.D.

211. [redacted]

[redacted]

[redacted] Both the H53_23-43 and H53_23-42 oligomers satisfy each element of claim 1 of the UWA Patents. *See supra* ¶¶ 39, 43, 67. Both H53_23-43 and H53_23-42 oligomers also satisfy each element of claim 1 of EP '781 Patent. *See supra* ¶161.

212. [redacted]

213. [redacted] was not submitted to the USPTO during prosecution of the NS Patents. Upon information and belief, the Examiner of the NS Patents was never informed [redacted]

IV. Inequitable Conduct Regarding the "Superiority" of Claimed Oligomers

A. Materiality of the Withheld Experimental Data

214. The USPTO allowed the '361 patent based on Mr. Zhengyu Feng's affirmative representation that a claimed oligomer, targeting positions 36-60 of Exon 53, exhibited "superior skipping activity over" a prior art oligomer reported in the '212 publication and the Popplewell paper, specifically, PMO-G targeting positions 30-59 of Exon 53. *See supra* ¶¶126-139. That representation occurred on at least two separate occasions, on July 22, 2016 and February 27, 2017, in response to the USPTO's Office Actions. *Id*., ¶¶133-34, 136-38.

[redacted]

215. Mr. Zhengyu Feng's representations [redacted] Neither Mr. Zhengyu Feng nor Mr. Watanabe submitted [redacted] *See supra* ¶208. [redacted] was not submitted to the USPTO before the issuance of the '361 patent or any of the NS Patents. *Id.*

216. Mr. Zhengyu Feng's representation to the USPTO also directly contradicts [redacted] was not disclosed to the USPTO before the issuance of the '361 patent or any of the NS Patents. *Id.*, ¶208.

217. But for this misrepresentation and the decision to withhold [redacted] the USPTO would not have allowed the '361 patent. If the USPTO had been aware of [redacted] it would not have allowed the '361 patent.

218. The materiality of the misrepresentation and [redacted] equally applies to each of the '092, '461, '106, '741, '217, and '322 patents. Each of the '092, '461, '106, '741, '217, and '322 patents is directed to substantially the same subject matter as the '361 patent—oligomers targeting positions 36 to 60 of exon 53. *See supra* ¶¶102-21. In view of the prosecution that led to the '361 patent, the USPTO allowed each of the '092, '461, '106, '741, '217, and '322 patents without any prior art rejection under 35 U.S.C. § 102 or § 103. *See supra* ¶140. Neither

[redacted] nor [redacted] conclusions [redacted] were submitted to the USPTO by Mr. Watanabe or Mr. Feng before the issuance of the '092, '461, '106, '741, '217, and '322 patents. *See supra* ¶208. But for the misrepresentation [redacted] the USPTO would not have allowed any of the NS Patents to issue.

B. Specific Intent to Deceive the USPTO

219. [redacted]

220. This was not the first time that Mr. Watanabe failed to disclose material information to a patenting authority. As described above, on multiple occasions, Mr. Watanabe [redacted] himself or NS at the Patent Offices in the United States, Japan, and Europe.

221. [redacted] Mr. Watanabe [redacted] in the specification of the NS Patents demonstrating that [redacted] *See supra* ¶¶200-201; *see also id.*, ¶¶190-99, 202-204.

[redacted]

222. [redacted] Mr. Watanabe [redacted] in the specification of the NS Patents demonstrating that [redacted]

223. [redacted] Mr. Watanabe [redacted] that contradicts the assertion that the "oligomer of the present invention is highly active than PMO-G" at the Japanese Patent Office. Mr. Watanabe also failed to provide his conclusions [redacted] to the Japanese Patent Office. *See supra* ¶¶157-159; *see also id.*, ¶¶205-208.

224. In his First and Second Declarations, Mr. Watanabe omitted [redacted] hat [redacted] *See supra* ¶¶209-13. The [redacted] Although Mr. Watanabe's First and Second Declarations were submitted to the USPTO during prosecution of each of the '092, '461, '106, '741, '217, and '322 patents, the [redacted] was never disclosed. *See supra* ¶213.

225. On information and belief, [redacted] Her law firm has been involved in various aspects of the NS Patents, including preparing and filing the underlying International PCT Application and prosecuting its Japanese counterpart patent in Japan. *See supra* ¶¶175-76, 157-59. [redacted] may not have directly communicated with the USPTO, she bears the same duty of candor as Mr. Feng and Mr. Watanabe. *See* 37 C.F.R. ¶

[redacted]

156(c) (duty to disclose material information extends to a person "who is *substantively involved* in preparation or prosecution of the application and who is *associated* with the inventor").

226. [redacted] NS would not have obtained the NS Patents. The single most reasonable inference from their pattern of failing to disclose [redacted] is that Mr. Watanabe and Mr. Feng intended to mislead the USPTO.

V. Inequitable Conduct Regarding the Sazani Paper

227. The claims of the NS Patents are directed to PMOs intended to be used as therapies for treating Duchenne Muscular Dystrophy. *See supra* ¶¶102-21. The specification of the NS Patents also proposes using PMOs as an "active ingredient" for treating muscular dystrophy. Ex. AC, 25:10-15 ("the present invention provides the pharmaceutical composition for the treatment of muscular dystrophy, comprising as an active ingredient the oligomer of the present invention, a pharmaceutically acceptable salt or hydrate thereof"). Information regarding the safety and genotoxicity of PMOs, especially those developed for treating Duchenne Muscular Dystrophy, is material to the claims of the NS Patents.

228. The Sazani paper provides non-cumulative, material information regarding the safety and genotoxicity of AVI-4658, a PMO developed to treat Duchenne Muscular Dystrophy. *See supra* ¶¶179-86. As shown in the Sazani paper, AVI-4658 carries the same 5'-end modification as the antisense oligomers later claimed by the NS Patents. *Id.*, ¶185. In other words, the Sazani paper confirmed the "high safety" of PMOs, including those with the exact chemical modifications claimed in the NS Patents. *Id.*, ¶¶183-85; *see also supra* ¶¶102-104. [redacted]

[redacted]

[redacted]

229. But Mr. Watanabe did not submit the Sazani paper to the USPTO during prosecution of the NS Patents. *See supra* ¶186. Had the USPTO been aware of the Sazani paper, along with the experimental data withheld from the USPTO, it would not have allowed the NS Patents to issue.

230. [redacted] Nevertheless, Mr. Watanabe withheld the Sazani paper from submission to the USPTO. *See supra* ¶186. The single most reasonable inference that can be drawn from Mr. Watanabe's nondisclosure of material information is that it was done with the intent to mislead the USPTO.

231. For at least the reasons set forth in the foregoing Paragraphs 96-230, the NS Patents are unenforceable due to inequitable conduct.

PRAYER FOR RELIEF

WHEREFORE, Sarepta and UWA respectfully request that the Court enter judgment in their favor and against Defendants on the counterclaims set forth above and respectfully requests that this Court:

[redacted]

1. award Sarepta the relief it seeks in its Defenses asserted in response to Nippon Shinyaku's Second Amended Complaint for Breach of Contract, Declaratory Judgment of Invalidity, and Patent Infringement;

2. deny all damages, costs, expenses, attorneys' fees, or other relief requested by Nippon Shinyaku;

3. enter judgment that the '851 patent has been infringed and will be infringed by Defendants, pursuant to at least 35 U.S.C. §§ 271(a), (b), and/or (c), either literally and/or under the doctrine of equivalents;

4. enter judgment that the '590 patent has been infringed and will be infringed by Defendants, pursuant to at least 35 U.S.C. §§ 271(a), (b), and/or (c), either literally and/or under the doctrine of equivalents;

5. enter judgment that the '827 patent has been infringed and will be infringed by Defendants, pursuant to 35 U.S.C. §§ 271(b) and/or (c), either literally and/or under the doctrine of equivalents;

6. to the extent that Defendants have or will commercially manufacture, use, offer for sale, or sell Viltepso within the United States or import Viltepso into the United States, prior to the expiration of the UWA Patents, including any extensions, enter judgment awarding Sarepta and UWA monetary relief pursuant to 35 U.S.C. § 284, together with interest;

7. enter judgment that Defendants' infringement of the UWA Patents has been willful, and/or an order increasing any damages awarded for Defendants' infringement of the UWA Patents pursuant to 35 U.S.C. § 284;

8. declare that Sarepta has not infringed and will not infringe any claim of the NS Patents;

[redacted]

9. declare that each claim of the NS Patents is invalid;

10. find that Nippon Shinyaku has knowingly, materially, and repeatedly breached the MCA's confidentiality and non-use provisions in bath faith and that those bad-faith breaches of the MCA constitute unclean hands, precluding Nippon Shinyaku from enforcing the MCA or obtaining injunctive or other equitable relief for any alleged breach of the MCA by Sarepta;

11. declare that the NS Patents are unenforceable, and that each asserted claim of the NS Patents is unenforceable, due to inequitable conduct;

~~11.~~12. declare that this is an exceptional case under 35 U.S.C. § 285 and award Sarepta and UWA their attorneys' fees, expenses, and costs; and

~~12.~~13. award all other and further relief the Court may deem just and proper.

DEMAND FOR A JURY TRIAL

Pursuant to Federal Rule of Civil Procedure 38(c), Sarepta and UWA hereby demand a trial by jury on all triable issues alleged in their counterclaims.

[redacted]

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~~March 21~~July 19, 2023

CERTIFICATE OF SERVICE

I hereby certify that on ~~,~~July 19, 2023, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on ~~,~~ July 19, 2023, upon the following in the manner indicated:

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